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BRITISH JOURNAL OF ANAESTHESIA

VOL. XXX, No. 7 JULY 1958

EDITORIAL

HALOTHANE

In this month's issue there are two papers on halothane and there are more to come in subsequent issues. It is too early to say with confidence what place, if any, halothane will take in the anaesthetics of the future. The first report of its use in clinical medicine appeared in this journal in September 1956 entitled "The human cardiovascular response to Fluothane", by M. Johnstone. Since that time, not yet two years ago, numerous reports have been published on the use of halothane as an anaesthetic. It would appear that those who have had the most extensive experience of it are the most enthusiastic. In what respects then does it differ from customary practice? In any attempt to get a fair and unbiased view it is necessary to go back some thirty years or so. Anaesthetists of that age will remember that their greatest difficulty was to secure adequate muscular relaxation in upper abdominal sections. It was a constant source of irritation and friction between surgeon and anaesthetist. The extensive use of spinal anaesthesia which followed on Pitkin's visit to this country put an end to this source of annoyance and the period 1930 to 1945 was a very happy one. However, all good things come to an end and about this latter year reports of rare but dramatic disasters following subarachnoid injection together with the advent of curare drastically reduced the use of spinal anaesthesia. Curare and the synthetic relaxants that soon followed it had many points in their favour. They were easy to give, could be repeated if necessary, and owing to their paralysing effect on the abdominal muscles maintained excellent relations between surgeon and anaesthetist. Having no anaesthetic qualities curare needed the assistance of other drugs to send the patient to sleep and to keep him free from pain. So following the use of the premedicants preferred by the anaesthetist a long list of drugs came into action to subserve the aforementioned functions. This use of a special drug for a specific purpose has in the minds of some anaesthetists being exalted to the rank of a fundamental principle. This attitude of mind is summed up by Armstrong Davison as follows: "While it is not disputed that it (halothane) may have some uses, it does not fit into the present trend of anaesthetic development, which is to produce narcosis, relaxation and other desired phenomena, by separate drugs each with a specific action, rather than return to the major use of agents with multiple effects. It therefore seems certain that, unless there be a great change in the line of evolution, it and similar drugs will play little part in the future of anaesthesia." But after all there is nothing sacrosanct in "the present trend". It may change, nay more, history teaches us it is certain to. Although perhaps relaxants are the latest important developments in anaesthesia they are certainly not the last. Even with the present trend no one will deny that there is a real need for a narcotic more potent than nitrous oxide that is noninflammable and devoid of effects other than narcosis. Such a drug may be a pharmacological impossibility, but at least the appearance of halothane shows that our research chemists are active and forward-looking and encourages us to anticipate future developments.

NEW MEMBER OF EDITORIAL BOARD

Dr. John W. Dundee, Director of Anaesthetics, Queen's University of Belfast, has been invited to join the Board of Management and Proprietors of the *British Journal of Anaesthesia*. We are glad to learn that he has accepted this invitation.

Brit. J. Anaesth. (1958), **30**, 302

THE EFFECT OF THIOPENTONE AND BUTHALITONE UPON THE QT INTERVAL IN THE ELECTROCARDIOGRAM

BY

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IN the normal electrocardiogram, the QRS complex is produced by the electrical changes due to ventricular excitation and contraction, whilst the T wave is produced by the ventricle returning to the resting, polarized state. Thus the period from the commencement of the Q wave to the finish of the T wave, the QT interval, corresponds to the period of ventricular systole. Bazett (1920) has confirmed this by the close relationship between figures for the duration of systole derived mechanically and electrically. He also noted that the QT interval varied inversely with the heart rate and he derived the following formula:

$$QT = K\sqrt{C}$$

where C = length of cycle in seconds and K = a constant whose average value was 0.37 for men and 0.40 for women.

Taran and Szilagyi (1947) have suggested that the QT interval may be conveniently standardized to a heart rate of 60 per min. This reduces the figure C in Bazett's formula to unity so that the corrected QT interval becomes the same as the figure K. It is usually designated by the symbol QTc.

Ashman and Hull (1945) have measured the QT interval in several thousand cases and have found that the average value for a heart rate of 60 per minute is 0.386 for men and children and 0.396 for women. They give the upper limits of normal as 0.422 and 0.432 respectively. Whilst quoting their own logarithmic formula for relating the QT interval to heart rate, they state that Bazett's formula is reasonably accurate for heart rates between 40 and 150 per minute.

In a comparison of thiopentone and buthalitone (Henderson and Mackett, 1958) where electrocardiograms were performed on 20 patients undergoing anaesthesia with each drug, it was discovered that the QTc was prolonged in every case. In this investigation, the electrocardiograms of 30 patients (15 with each thiobarbiturate) have been analyzed and the QT intervals measured. After examination of the results from these cases, a small additional series of 5 cases, having buthalitone in half the dosage of the first series, was included.

METHOD

All patients were aged 10 years or over and were selected at random. The majority were outpatients and some are from the series of 40 previously described (Henderson and Mackett, 1958). The duration of operation varied from 10 to 15 minutes. The age and sex of the patients are shown in table I. No patient had any history or signs of cardiac disease.

TABLE I
Age and Sex of Patients.

	Buthalitone 70 mg per stone (10.9 mg/kg)	Thiopentone 35 mg per stone (5.5 mg/kg)
Age—average	29.8	30.4
limits	10–56	14–49
Males	4	9
Females	11	6
Total	15	15

All patients were premedicated with 0.64 mg of atropine given half an hour before operation.

A control electrocardiogram of leads I, II and III and the augmented limb leads AVR, AVL and AVF was performed just before induction of anaesthesia. From this, the lead producing the most clearly defined T waves was selected and this lead was used for all subsequent observations. In 4 cases, an additional tracing was made before the premedication had been given in order to

determine whether atropine produced any effect upon the QTc.

Buthalitone was used by the technique of Henderson and Mackett (1957) where a single induction dose at the rate of 70 mg per stone (10.9 mg per kg) body weight was followed by maintenance with nitrous oxide, 8 l./min, and oxygen, 2 l./min. Thiopentone was used in a dosage of 35 mg per stone (5.5 mg per kg) body weight as this rate was found by Henderson and Mackett (1958) to give an equivalent anaesthetic effect when used by the same technique as that for buthalitone.

The thiobarbiturate was injected as rapidly as possible and a continuous tracing was made during and for 30 seconds following induction. The facemask was then applied and the nitrous oxide-oxygen mixture administered.

Further tracings were made after 1, 5 and 10 minutes from the start of the injection. A final tracing was made as soon as the patient was awake.

In a few cases, anaesthesia was insufficient and had to be supplemented with intermittent doses of suxamethonium chloride. This agent was chosen as it was found to have no effect upon the electrocardiogram and in fact improved the tracing by the abolition of skeletal muscle interference.

Measurement of QTc.

The QT interval is measured from the start of the Q wave to the finish of the T wave and the length of the cardiac cycle is calculated from the preceding R-R interval. All times were measured to the nearest 0.02 sec.

As there were considerable variations of the heart rate between patients and also in the same patient during the course of the anaesthesia, it was decided to standardize all figures to the QTc. This was facilitated by the use of the nomogram of Kissin et al. (1948) which is based on Bazett's formula. The QTc was calculated for not less than three separate measurements and the final figure is an average of these.

RESULTS

The results of the main series are shown in table II and appendix I. It will be noticed that the initial average value of QTc in the buthalitone series, 0.397, is higher than that of the thiopentone series which is 0.389. This is attributed to the greater number of females in the former series. However, when tested statistically, this difference is not significant ($t=0.39$).

TABLE II

Main Series: Average QTc's in seconds.

Time	Buthalitone 70 mg per stone (10.9 mg/kg)	Thiopentone 35 mg per stone (5.5 mg/kg)
Control	0.397	0.389
During injection	0.441	0.414
30 sec	0.444	0.442
1 min	0.455	0.427
5 min	0.454	0.414
10 min	0.429	0.409
Recovery	0.406	0.410

In order to be able to compare these results, each QTc value was calculated as a percentage of the initial QTc of that patient (appendix II) and the means of these percentage values are given in table III. In both series, the mean percentage increase in the QTc at 30 seconds is statistically significant at the 0.1 per cent level (buthalitone series, $t=9.81$; thiopentone series, $t=6.39$).

TABLE III

Main Series: QTc expressed as the average of the percentage increase over the control readings for each case.

Time	Buthalitone 70 mg per stone (10.9 mg/kg)	Thiopentone 35 mg per stone (5.5 mg/kg)
Control	100	100
During injection	111.45	106.47
30 sec	112.04	114.05
1 min	114.59	110.27
5 min	114.70	106.85
10 min	108.36	105.50
Recovery	102.05	105.82

Figure 1 demonstrates that the rise in QTc produced by thiopentone is maximal at 30 seconds after the start of the injection and then there is a rapid fall. Buthalitone produces a slightly greater increase which is almost maximal at 1 minute after the start of the injection and is sustained until 5 minutes, when it falls more slowly to normal.

If the maximal percentage increases of the QTc for each case are averaged for each series, there is

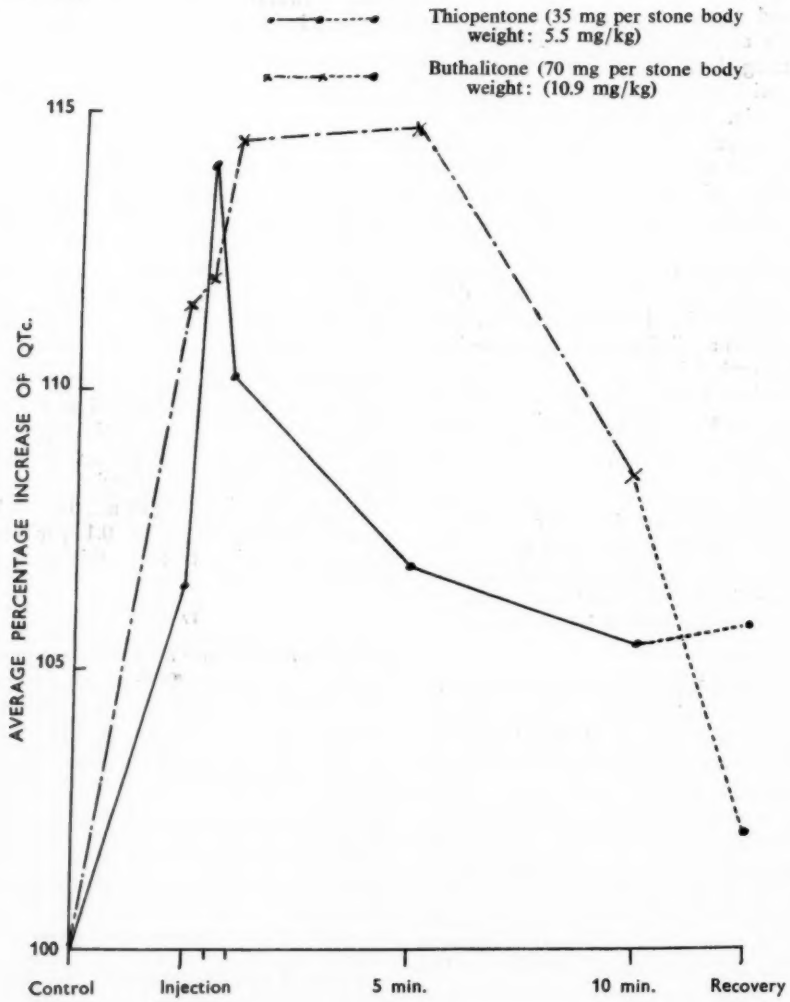

FIG. 1

Main series average of percentage increases of QTc.
(Interrupted lines between 10 min and full recovery indicate that this period is variable.)

a greater increase with 70 mg per stone of buthalitone than with 35 mg per stone of thiopentone. This is shown in table IV. This difference is significant at the 5 per cent level ($t=2.34$).

TABLE IV
Maximal Percentage Increases of QTc.

Buthalitone 70 mg per stone (10.9 mg/kg)	Thiopentone 35 mg per stone (5.5 mg/kg)
139.43	107.32
127.16	105.81
132.93	114.47
127.03	109.52
122.51	111.84
118.61	130.30
126.83	122.22
120.00	126.83
107.31	116.22
116.87	111.39
106.17	121.79
110.84	122.35
104.65	117.45
130.86	107.06
137.84	114.28
Mean 122.00	Mean 116.06

Significance of difference of means.
$t=2.34$
Significant at 5% level

Following examination of these results, it was decided to include an additional series in which buthalitone was given at the same rate of dosage (35 mg per stone body weight i.e. 5.5 mg/kg) as that of thiopentone in the main series. This series was limited to 5 cases as the reduced rate of dosage of buthalitone was only just sufficient to produce sleep and all 5 cases required supplementing with suxamethonium chloride. The average QTc's of these cases are shown in table V together with the means of the percentage increase of QTc for each case. These results are compared with the thiopentone series in figure 2. They suggest that, in a dosage of 35 mg per stone, buthalitone has not as potent a cardiac effect as thiopentone in similar dosage although, in a dosage of 70 mg per stone (the clinically equipotent dose—Henderson and Mackett, 1958) it has a greater and more prolonged effect on the heart than 35 mg per stone of thiopentone. When the average percentage increases of QTc in the additional buthalitone series are compared with those of thiopentone there is no significant difference. This may be due to the small size of the buthalitone series. It also demonstrates that the effect of the drug on the heart is a quantitative one depending upon the amount of drug given in terms of the size of the patient (fig. 3).

TABLE V
Results of the Additional Buthalitone Series.

Time	Buthalitone 35 mg per stone (5.5 mg/kg)	
	Average QTc in sec	Average of percentage increases
Control	0.397	100
During injection	0.417	105.41
30 sec	0.428	108.08
1 min	0.430	108.27
5 min	0.406	102.51
10 min	0.406	102.54
Recovery	0.401	101.17

In 4 patients, electrocardiograms were performed before the premedication had been given. The QTc for these cases before premedication, before induction and during recovery are shown in table VI. These results show that, in 3 out of the 4 cases, there is prolongation of the QTc before induction as compared with the figure before premedication. In the other case, there was little difference between the two figures. However, the QTc in this case during recovery was much less than those before anaesthesia. When tested for significance, these differences between the QTc before and after premedication and during recovery were not significant ($t=1.48$).

It had been suggested that the toxaemia due to sepsis may prolong the QTc. However, the average control QTc for 19 patients with septic lesions was 0.393 while that for the remaining 11 patients in the main series was 0.392.

TABLE VI
Four Cases where the QTc was recorded before the Premedication had been given.

QTc in sec		
Before premedication	Before induction	Recovery
0.370	0.410	0.370
0.375	0.415	0.390
0.410	0.405	0.360
0.370	0.415	0.440

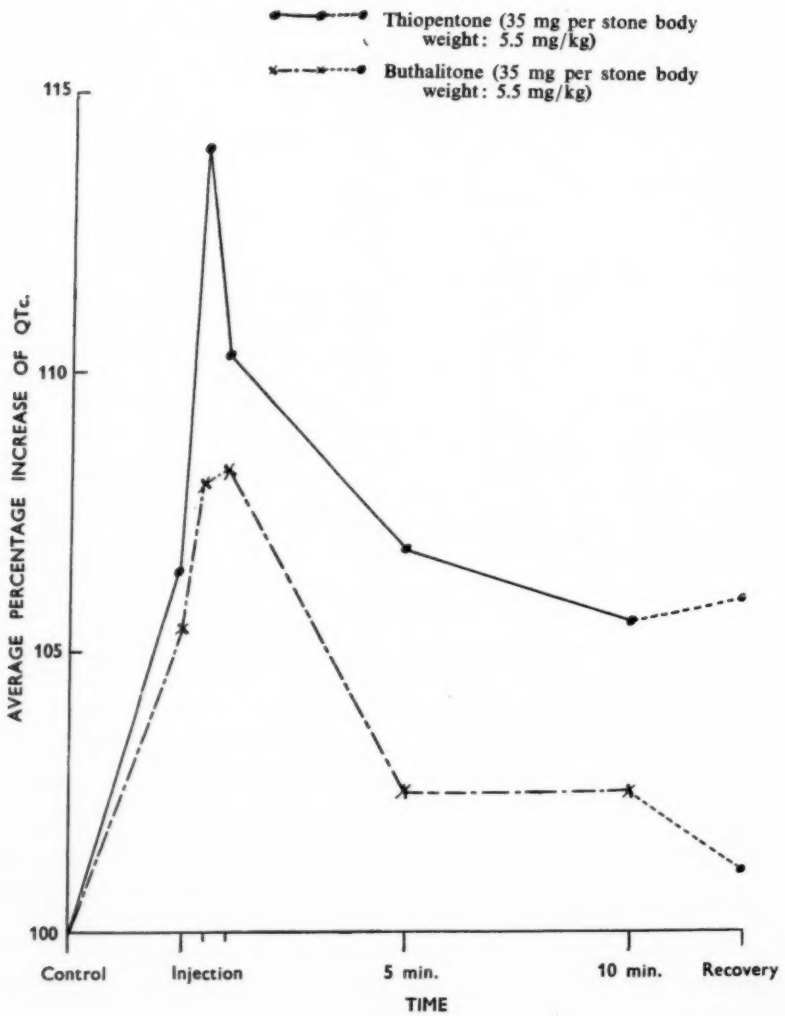

FIG. 2

Additional buthalitone series compared with the thiopentone series. (Interrupted lines between 10 min and full recovery indicate that this period is variable.)

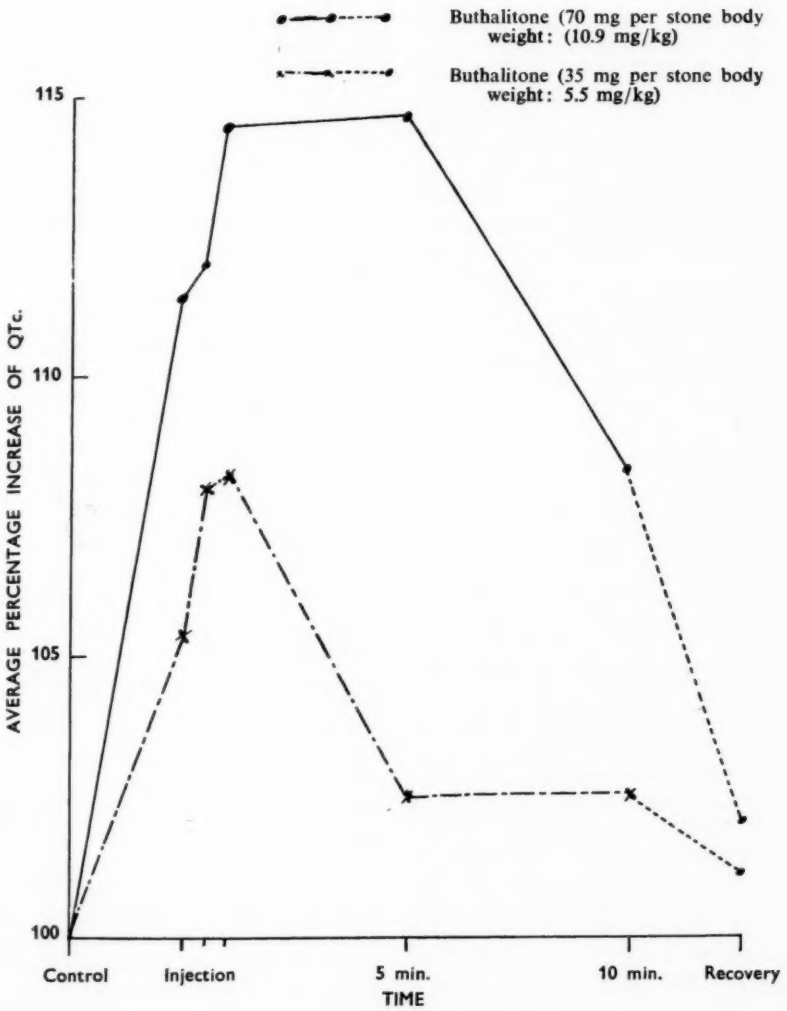

FIG. 3

Additional buthalitone series compared with the main buthalitone series. (Interrupted lines between 10 min and full recovery indicate that this period is variable.)

DISCUSSION

Since Bazett's work (1920) the QT interval had little clinical application until Taran and Szilagyi (1947) observed that prolongation occurred with rheumatic carditis in children and that serial observations of the QTc provided a valuable means of assessing the progress of this condition. Taran and Szilagyi (1951) postulate that a raised QTc is a sign of impairment of the functional integrity of the myocardium. However, their view of the importance of the QTc in rheumatic carditis is not shared by all physicians and there are many who attach little significance to it.

Other factors which prolong the QTc are myocardial infarction, congestive failure, hypocalcaemia and hypopotassaemia, while digitalis shortens it (Suffern, 1956). Wiggers and Clough (1919) found consistently that prolongation of systole was significant of functional cardiac disorder.

The QTc may also be prolonged by endogenous sympathetic stimulation and adrenaline release such as occurs in nervousness. This will perhaps explain the case in table VI (a nervous girl aged 10 years) where the QTc before premedication and before induction was prolonged as compared with the value during recovery. Atropine also appears to prolong the QTc although this effect may be due to nervousness before induction causing sympathetic stimulation.

Rollason and Hough (1957) have reported on the electrocardiographic changes produced by intubation and inflation of the cuff. A prolongation of QTc occurred in 5 cases and this was attributed to sympathetic stimulation and to the vagolytic action of gallamine triethiodide. Shortening of the QTc was observed in 9 cases and this was thought to be due to vagal stimulation. In a subsequent paper these workers (Rollason and Hough, 1958) report on a series of 52 cases where electrocardiograms were performed before and 2 minutes after induction of anaesthesia with thiopentone. Increase of QTc of 0.04 sec or more was observed in 16 cases and a shortening of 0.04 sec in 2 cases. Changes of less than 0.04 sec were not recorded.

At first sight, these results of Rollason and Hough (1958) might seem to conflict with our finding that prolongation of the QTc occurred in every case induced with thiopentone. However, our serial observations of QTc shortly after induction show that the maximum increase with thiopentone occurs at 30 seconds after injection and that it would be decreasing rapidly at 2 minutes after injection. When our figures for QTc at 1 minute after injection are analyzed for the 15 thiopentone cases, only 9 cases have their QTc prolonged by 0.04 sec or more while 1 case has a QTc of 0.03 sec less than the control value. No doubt, had we taken recordings at 2 minutes after injection, fewer cases would have exceeded the 0.04 sec limit and the proportions would have been comparable with Rollason and Hough's series. An additional factor may be that their dosage of thiopentone was not constant, varying from 2.9 to 8.6 mg per kg body weight (as compared with our fixed rate of 5.5 mg per kg body weight), the lower dosage rate perhaps being insufficient to prolong the QTc beyond their limit of 0.04 sec.

As mentioned in the introduction to this paper, we had observed a prolongation of the QTc in all electrocardiograms recorded during anaesthesia with thiopentone and buthalitone. It therefore occurred to us that this measurement might be used as a means of obtaining information as to the degree of toxicity of anaesthetic drugs upon the myocardium. With this in view, we proceeded to record electrocardiograms on 30 cases (15 with each drug) so that a comparison could be obtained. The results (fig. 1) show that, with equipotent dosage (Henderson and Mackett, 1958), the effect of buthalitone given at a rate of 70 mg per stone body weight is much greater than that of thiopentone given at half this rate of dosage.

We also considered the possibility that this difference might be associated with the dosage used. In order to determine whether this was so, a series of 5 cases was given buthalitone in half the dosage of the main series which was the same dosage as the thiopentone series. A similar set of electrocardiograms was recorded and the results of this small series are compared with those of the thiopentone series in figure 2. This shows that the two graphs now tend towards the same shape although, with this dosage of buthalitone, the percentage increase in the QTc is less. Also the anaesthesia was insufficient and had to be sup-

plemented with suxamethonium chloride in every case.

This would seem to confirm our hypothesis that the greater rise in QTc with buthalitone in the original series was associated with a higher rate of dosage (by weight). It would also suggest that this measurement with a cardiotoxic drug would bear some direct relationship to the concentration of that drug in the blood and therefore its dosage. The degree of prolongation of the QTc may therefore be a useful measure of cardiac toxicity and we feel that it merits further investigation from this aspect.

SUMMARY

Electrocardiograms have been performed upon 30 patients undergoing anaesthesia with buthalitone and thiopentone in equipotent dosage. Buthalitone was found to produce a greater and more sustained prolongation of QTc than thiopentone.

A small series of 5 cases received buthalitone in half the original dosage and which was the same rate of dosage as the thiopentone series. This buthalitone series had a rise of QTc more comparable to that of the thiopentone series. This also demonstrated that the effect of a drug on the QTc is related to its rate of dosage.

The view is put forward that the measurement of the QTc may be an index of the cardiotoxicity of a drug, but there is, as yet, insufficient evidence to support this contention.

ACKNOWLEDGMENTS

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APPENDIX I

Results of each case expressed as QTc in seconds.

No.	Sex	Age	Before atropine	Control	During injection	30 sec	1 min	5 min	10 min	Recovery
Buthalitone			70 mg per stone (10.9 mg/kg) body weight							
1	F	39	—	0.355	0.505	0.455	0.490	0.495	0.480	0.465
2	F	29	—	0.405	0.465	0.460	0.460	0.490	0.515	0.430
3	F	37	—	0.410	0.435	0.420	0.490	0.545	0.470	0.430
4	F	30	—	0.370	0.370	0.405	0.420	0.470	0.400	0.390
5	M	18	—	0.355	0.460	0.435	0.410	0.400	0.380	0.360
6	F	23	—	0.430	0.440	0.450	0.510	0.450	0.390	0.450
7	M	25	0.370	0.410	0.425	0.460	0.490	0.520	0.400	0.370
8	F	43	—	0.375	0.410	0.400	0.425	0.450	0.430	0.410
9	F	25	—	0.410	0.400	0.440	0.440	0.430	0.435	0.410
10	F	23	0.375	0.415	0.490	0.485	0.470	0.420	0.450	0.390
11	F	10	0.410	0.405	0.430	0.390	0.380	0.410	0.430	0.360
12	F	19	0.370	0.415	0.480	0.460	0.460	0.460	0.420	0.440
13	F	36	—	0.430	0.460	0.440	0.440	0.440	0.450	0.400
14	M	21	—	0.405	0.450	0.450	0.530	0.435	0.420	0.400
15	M	56	—	0.370	0.400	0.510	0.405	0.400	0.370	0.370
Thiopentone			35 mg per stone (5.5 mg/kg) body weight							
1	F	44	—	0.410	0.490	0.440	0.390	0.405	0.430	0.430
2	M	24	—	0.430	0.425	0.430	0.455	0.410	0.440	0.430
3	M	35	—	0.380	0.375	0.435	0.390	0.380	0.400	0.375
4	F	28	—	0.420	0.430	0.430	0.460	0.430	0.390	0.410
5	M	44	—	0.380	0.405	0.425	0.425	0.410	0.420	0.410
6	M	27	—	0.330	0.340	0.430	0.390	0.360	0.365	0.360
7	M	44	—	0.360	0.370	0.440	0.410	0.400	0.385	0.360
8	F	49	—	0.410	0.465	0.520	0.465	0.475	0.425	0.450
9	M	21	—	0.370	0.420	0.400	0.430	0.405	0.365	0.400
10	M	26	—	0.395	0.420	0.440	0.410	0.410	0.430	0.415
11	F	21	—	0.390	0.410	0.440	0.475	0.455	0.410	0.420
12	F	19	—	0.425	0.470	0.520	0.490	0.450	0.440	0.450
13	M	25	—	0.360	0.405	0.430	0.410	0.420	0.420	0.420
14	F	36	—	0.425	0.440	0.455	0.430	0.430	0.430	0.440
15	M	14	—	0.350	0.350	0.400	0.380	0.380	0.390	0.390
Buthalitone			35 mg per stone (5.5 mg/kg) body weight							
A	F	43	—	0.420	0.430	0.430	0.440	0.410	0.390	0.385
B	F	42	—	0.405	0.395	0.410	0.500	0.420	0.420	0.420
C	M	55	—	0.390	0.390	0.410	0.430	0.430	0.440	0.390
D	M	14	—	0.420	0.450	0.475	0.420	0.400	0.410	0.440
E	M	43	—	0.350	0.420	0.415	0.360	0.370	0.370	0.370

Each reading is the average of not less than 3 separate measurements and is expressed to the nearest 0.005 of a second.

APPENDIX II

Results of each case expressed as a percentage of the control QTc.

No.	Before atropine	Control QTc	During injection	30 sec	1 min	5 min	10 min	Recovery
Buthalitone.		70 mg per stone (10.9 mg/kg) body weight.						
1	—	0.355	142.25	128.77	138.02	139.43	135.21	130.79
2	—	0.405	114.81	113.58	113.58	120.99	127.16	106.17
3	—	0.410	106.10	102.44	119.51	132.93	114.63	104.88
4	—	0.370	100.00	109.46	113.13	127.03	108.11	105.41
5	—	0.355	129.58	122.51	115.49	112.68	107.04	101.41
6	—	0.430	102.33	104.65	118.61	104.65	90.70	104.65
7	90.24	0.410	103.66	112.19	119.51	126.83	97.56	90.24
8	—	0.375	109.33	106.67	113.33	120.00	114.67	109.33
9	—	0.410	97.56	107.31	107.31	104.88	106.10	100.00
10	90.36	0.415	118.07	116.87	113.25	101.20	108.43	93.97
11	101.23	0.405	106.17	96.29	93.33	101.23	106.17	88.89
12	89.16	0.415	115.66	110.84	110.84	110.84	101.20	106.02
13	—	0.430	106.98	102.33	102.33	102.33	104.65	90.02
14	—	0.405	111.11	111.11	130.86	107.41	103.70	98.76
15	—	0.370	108.11	137.84	109.46	108.11	100.00	100.00
Thiopentone.		35 mg per stone (5.5 mg/kg) body weight.						
1	—	0.410	119.51	107.32	95.12	98.78	104.88	104.88
2	—	0.430	98.84	100.00	105.81	95.35	102.33	100.00
3	—	0.380	98.69	114.47	102.63	100.00	105.26	98.69
4	—	0.420	102.38	102.38	109.52	102.38	92.86	98.62
5	—	0.380	106.58	111.84	111.84	107.90	110.53	107.90
6	—	0.330	103.03	130.30	118.18	109.09	110.61	109.09
7	—	0.360	102.78	122.22	113.89	111.11	106.95	100.00
8	—	0.410	113.41	126.83	113.41	115.85	103.66	109.75
9	—	0.370	113.51	108.11	116.22	109.46	98.65	108.11
10	—	0.395	106.33	111.39	103.80	103.80	108.86	105.06
11	—	0.390	105.13	112.81	121.79	116.67	105.13	107.69
12	—	0.425	110.59	122.35	115.29	105.88	103.53	105.88
13	—	0.360	112.50	119.45	113.89	116.67	116.67	116.67
14	—	0.425	103.53	107.06	101.17	101.17	101.17	103.53
15	—	0.350	100.00	114.28	108.57	108.57	111.43	111.43
Buthalitone.		35 mg per stone (5.5 mg/kg) body weight.						
A	—	0.420	102.38	102.38	104.76	97.62	92.86	91.67
B	—	0.405	97.53	101.23	123.45	103.70	103.70	103.70
C	—	0.390	100.00	105.13	110.26	110.26	112.81	100.00
D	—	0.420	107.14	113.10	100.00	95.24	97.62	104.76
E	—	0.350	120.00	118.57	102.86	105.71	105.71	105.71

Brit. J. Anaesth. (1958), **30**, 312

HALOTHANE CONCENTRATION FROM A ROWBOTHAM'S BOTTLE IN A CIRCLE ABSORPTION SYSTEM

BY

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For the preacher's merit or demerit
It were to be wished that the flaws were fewer
In the earthen vessel holding treasure
But the main thing is, does it hold good measure.
Heaven soon sets right all other matters.
ROBERT BROWNING (*Christmas Eve* 1850)

A NUMBER of reports have been published concerning vaporizers for halothane (Johnstone, 1956, 1957; Bryce-Smith and O'Brien, 1956; Mapleson, 1957; Epstein, 1957; Falkner Hill, 1957, 1958; Brennan, 1957) but the majority of them depend upon a semiclosed nonabsorption technique and some involve the purchase of special apparatus; these methods are therefore costly, with halothane at its present price of about ten pounds sterling for one pound avoirdupois.

Marrett (1957) was the first to point out that halothane can be administered satisfactorily in a closed circuit and later Brennan, Hunter and Johnstone (1957) recommended a modified Waters to-and-fro absorption technique using a Fluotec vaporizer, but they admit that they are suspicious of a circle absorber in view of a possible rapid build-up of a lethal vapour concentration; nevertheless Gusterson (1957) had stated that satisfactory results can be obtained in a circle system using a standard Rowbotham's bottle as the vaporizer, but he gave no evidence at the time for his statement and this paper is presented in support of his contention.

After over a year's clinical trial involving more than 500 selected cases it was decided to measure, by infrared gas analysis, the concentration of halothane inspired by the patient during operations of up to one and a half hours duration. This time limit was imposed for a number of reasons, two of the more important being:

(1) After such time the level of halothane in Rowbotham's bottle, henceforth known as the "bottle", had fallen to below the metal wick.

(2) In the present state of our knowledge it was thought wise to limit the administration to under two hours.

It must be admitted that to insert a bottle into the inspiratory side of a circle absorber involved some increase of resistance to inspiration, but in spite of repeated attempts to measure this with a water manometer during operations, no positive evidence could be obtained, possibly due in part to the fact that respiration under halothane anaesthesia is shallower and smoother than with most other volatile anaesthetics. There is no doubt that the design of the bottle (used for this purpose) could be improved and this is under consideration at the present time.

METHOD OF GAS ANALYSIS

Premedication and induction of anaesthesia in 25 selected routine operation cases was standardized as far as possible for the tests. Atropine 1.5 mg with or without morphia 10 mg were given one hour pre-operatively and anaesthesia induced with small amounts of thiopentone 200–500 mg. All the patients were intubated with a cuffed Magill endotracheal tube following an intravenous injection of suxamethonium 50–75 mg, pethidine 15–25 mg and spraying of the cords and trachea with 4 per cent lignocaine. Anaesthesia was maintained with nitrous oxide/oxygen at 2 litres/1 litre or oxygen only, at 1 litre per minute, passing into a standard B.O.C. circle absorption unit, to which was attached a Rowbotham's bottle containing 25 ml of halothane at theatre temperature, on the inspiratory side next to the flap valve. An intentional leak was permitted through the expiratory valve.

A small electric pump was used to draw off gases from the inspiratory conduit at the rate of ½–1 litre per minute and to pass them through a metal tube into an infrared gas analyzer especially calibrated to register concentrations of halothane of up to 3 per cent. The gases once analyzed were returned to the expiratory side of the circuit.

Three sampling points were used during the experiments:

Point A. Immediately distal to the bottle.

Point B. Two-thirds of the way along the inspiratory tubing of the circle absorber.

Point C. The endotracheal connection.

Readings were obtained for various settings of the vaporizer, for the two flow rates mentioned above and for both unaided and controlled respiration.

The zero setting of the analyzer was continuously checked and calibrated against a known concentration of halothane in air (3 per cent).

It was found that nitrous oxide and carbon dioxide in the circuit gave an error of 0.15 per cent but this was ignored. Water vapour did not affect the readings in any way.

As this investigation was undertaken more from a clinical standpoint than a laboratory one, it was considered that accuracy to the nearest 0.25 per cent would be acceptable to even the most meticulous of practising anaesthetists.

Readings were taken continuously throughout the anaesthesia at intervals of 2–3 minutes and 30–60 seconds after any alteration in either the lever setting, gas flow rate or type of respiration.

RESULTS

In order to avoid any confusion over the interpretation of the results obtained, graphs (figs. 1–4) were made from average readings with two standard bottles (used alternately) and tapping sampling point B. Readings taken from point A tended to be nearly 0.25 per cent higher and readings from point C were nearly 0.25 per cent lower due to dilution with the expired gases.

The phenomenon reported by Mapleson (1957) of a momentary initial kick in concentration, when the tap on the vaporizer was first turned on at the beginning of anaesthesia, was confirmed, but no concern was felt for this event as readings obtained from points A and C showed that dilution and possibly rubber absorption had minimized this effect by the time the gases reached the patient.

Variation of the tap settings at any time during the first hour, with or without change in either the new gas flow rate or type of respiration, gave remarkably constant readings on the analyzer (see table I). At no time was there a build-up of concentration of halothane in the circuit; on the contrary, after about one hour of unaided respiration or half an hour of controlled respiration there was a decrease of about 0.25 per cent (see table II).

It was only possible to achieve a concentration in excess of 3 per cent in one set of circumstances, when the bottle was turned full on, the flow rate of new gases minimal and controlled respiration used; such an occasion was never found necessary in the past year's clinical trial nor in fact since, unless halothane was being used deliberately as a hypotensive agent comparable in degree to trimetaphan. This use of the drug, in the state of present knowledge, is not recommended.

The temperature of halothane in the vaporizer fell a maximum of 10°F after 1½ hours or after 15 ml of the liquid had been vaporized.

It was usual to use halothane at the rate of about 10 ml per hour for unaided respiration and double this rate in my hands for controlled respiration.

Refilling the vaporizer after 1–1½ hours did give slightly higher readings of a fluctuant nature for some 3–5 minutes but the explanation and description of these readings do not come within the scope of this paper.

SUMMARY AND CONCLUSIONS

From infrared gas analysis of the halothane concentration in the inspired gases in a circle absorption system with some 25 selected operation cases and after a clinical trial of more than 500 patients it is shown that, using a standard Rowbotham's bottle in the circuit as the vaporizer, satisfactory and safe concentrations of halothane could be obtained and held for periods up to one and a half hours; furthermore there was no evidence of a build-up of concentration in the system nor was it possible to deliver to the patient concentrations in excess of 3.5 per cent.

The method described is economical and does not involve the purchase of expensive apparatus.

The figures presented are factual for the usual

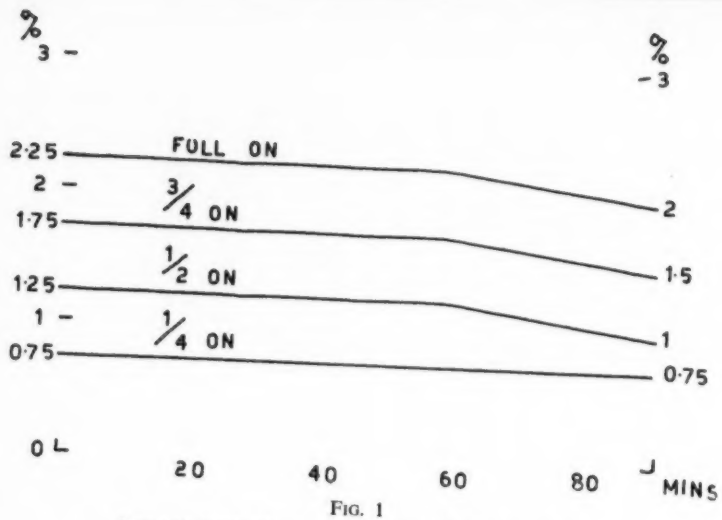

FIG. 1

Unaided respiration. 3 litres/min new gas flow.

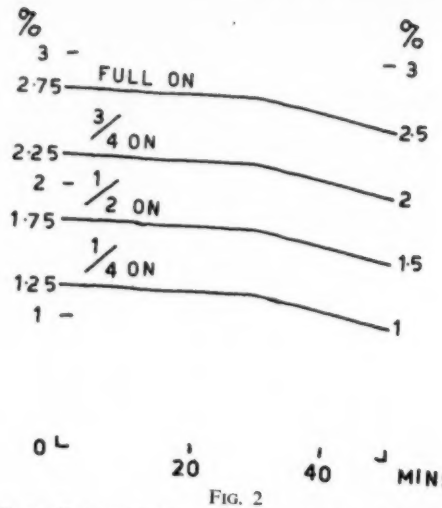

FIG. 2

Controlled respiration. 3 litres/min new gas flow.

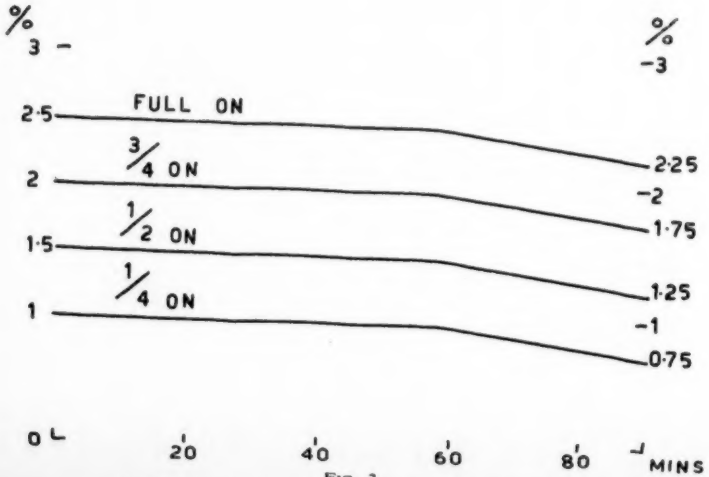

FIG. 3

Unaided respiration. 1 litre/min new gas flow

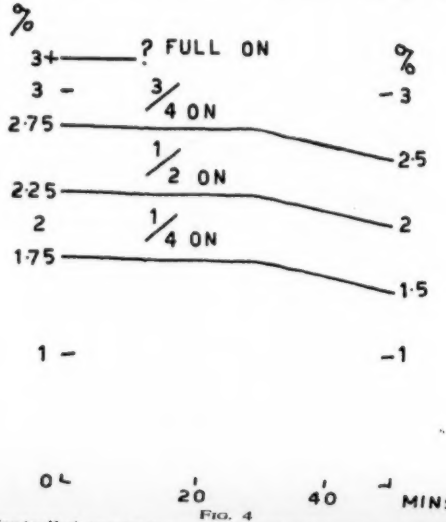

FIG. 4

Controlled respiration. 1 litre/min new gas flow

TABLE I

Specimen readings obtained during an operation for varicose veins.

Minutes from start of anaesthesia	Rowbotham bottle setting	Type of respiration	New gas flow rate in litres	Percentage halothane from analyzer	Percentage halothane from figures 1–4	Temperature of halothane	Halothane used in ml
0	Off	Unaided	3	0.15	0	72°F	0
5	¼	,,	3	1.75	1.75		
9	¼	,,	3	1.7	1.75		
12	Full	,,	3	2.2	2.25		
15	½	,,	3	1.2	1.25		
16	½	,,	1	1.45	1.5		
17	½	,,	3	1.35	1.25		
18	¼	,,	3	1.8	1.5		
20	Full	,,	3	2.2	2.25		
21	Full	Controlled	3	2.85	2.75		
22	Full	,,	1	3+	3+		
25	½	,,	1	2.0	2.25		
26	¼	Unaided	3	0.75	0.75		
27	¼	,,	3	0.75	0.75		
29	½	,,	3	1.35	1.25		
31	½	Controlled	3	1.8	1.75		
33	½	,,	3	2.0	1.75		
36	½	Unaided	3	1.3	1.25		
38	½	,,	3	1.45	1.25		
40	¼	,,	3	1.7	1.75		
42	¼	,,	3	2.4	2.25		
43	¼	Controlled	3	2.5	2.25		
49	¼	,,	3	0.65	0.75		
55	¼	Unaided	3	0.7	0.75		
59	Off	,,	3	0.5	—	65°F	11

TABLE II

Specimen readings obtained during an operation for hemicolectomy after 60 minutes of controlled and unaided respiration.

Minutes from start of anaesthesia	Rowbotham bottle setting	Type of respiration	New gas flow rate in litres	Percentage halothane from analyzer	Percentage halothane from figures 1–4	Temperature of halothane	Halothane used in ml
61	¼	Unaided	3	0.85	0.75	67°F	12
65	¼	,,	1	1.0	1.0		
68	¼	Controlled	1	1.45	1.5		
71	½	,,	1	1.75	2.0		
73	½	,,	1	2.0	2.0		
78	¼	Unaided	1	0.9	0.75		
80	Off	,,	3	0.6	—	64°F	16

operating theatre conditions in this country, i.e. in conditions where the temperature range is 72–75°F.

ACKNOWLEDGMENTS

I am indebted to the Infra Red Development Company for the loan of a specially constructed and calibrated direct reading infrared gas analyzer and to Dr. H. G. Epstein of Oxford, and Mr. D. W. Hill of the Anaesthetic Laboratory, Royal College of Surgeons, for advice and encouragement.

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ERRATA

The following corrections should be made to the paper on "Decamethonium Iodide; A Reappraisal" by J. I. Murray Lawson in the May 1958 issue (*Brit. J. Anaesth.*, **30**, 240):

(*1*) *page 240, column 2, lines 6 and 7, should read:*

". . . to be unreliable and indeed dangerous, owing to their hypotensive action." . . . .

(*2*) *page 241, column 1, line 19, should read:*

". . . following an induction dose of up to 750 mg thiopentone, . . ."

Brit. J. Anaesth. (1958), **30**, 317

THE COMPARATIVE POTENCIES OF BUTHALITONE AND THIOPENTONE IN OUT-PATIENT ANAESTHESIA

BY

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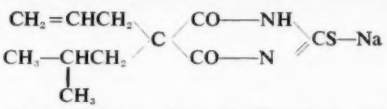
THIOPENTONE was introduced to clinical anaesthesia by Lundy in 1934 and the first reports of its use appeared in the following year (Lundy, 1935; Lundy and Tovell, 1935). Since then, thiopentone has almost entirely superseded other intravenous agents and has become the standard agent for inducing anaesthesia. It is not, however, without certain dangers. The main disadvantages are the occasional occurrence of laryngeal spasm (Lee, 1953; Dundee, 1956) and the ease with which respiratory depression due to overdosage can be produced. Another objection to thiopentone is that, following induction and a brief period of anaesthesia, the patients often have a relatively prolonged period when they are drowsy and confused and in a state described by Lundy (1935) as resembling alcoholic inebriation.

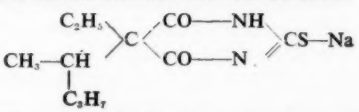
Research workers have been constantly seeking other similar drugs which would show a shorter recovery period with less postanaesthetic confusion, and buthalitone was introduced as such a drug. Claims have also been made that the incidence of respiratory depression and vagotonic effects is less with this drug than with thiopentone (Davidson and Love, 1956).

Buthalitone was first prepared by Miller et al. (1936) but it was not used clinically until 1954 when Weese and Koss reported on a clinical trial of 350 cases. This has been followed by numerous reports of other clinical trials in which this drug has been used (Dietmann, 1954; Pestel, 1954; Vollmer and Haaf, 1954; Ritter and Schäffer, 1954; Bergentz and Arosenius, 1955; De Cesare and Paoletti, 1955; Nobes, 1955a, b; Ruddell, 1955; Westerborn and Stenberg, 1955; Guldmann, 1956; Manni et al., 1956; Rajagopalan, 1956; Williams, 1956; Young, 1956; Duffield and Ginsberg, 1957; Mostert and Durham, 1957). Following our investigation into the use of buthalitone sodium in out-patient anaesthesia (1957), it seemed to us to be reasonable to try using thiopentone under similar conditions and to see whether the claims for buthalitone could be substantiated and to make a comparison between the two drugs.

Both buthalitone and thiopentone are thiobarbiturates, the former being sodium 5-allyl-5-isobutyl-2-thiobarbiturate having the formula:



while the latter is sodium 5-ethyl-5-(1-methylbutyl)-2-thiobarbiturate with the formula:



and, like most thiobarbiturates, they resemble each other both physically and chemically. Several comparisons of the two drugs have been published and these include experiments in rats, dogs and rabbits by Gruhzit et al. (1937) and in rabbits by Irmer (1955). However, it is sometimes difficult to correlate these findings resulting from animal experiments with those obtained in man due to variations in the response to any given drug between different species. We have therefore confined our investigation and discussion to the comparison of these two drugs in man.

One of the first reports of such a comparison was by Freuchen (1956) who compared two series, each of 100 cases; one series having been given thiopentone and the other buthalitone. Most of these patients, who were undergoing various operations, were premedicated with morphine 10 mg and scopolamine 0.4 mg. Using the drugs for

induction and maintenance as required, he found that the average total doses were 15.1 mg per kg body weight (96 mg/stone body weight) for buthalitone and 8.3 mg per kg body weight (52.8 mg/stone body weight) for thiopentone. The average recovery times were 15.7 minutes for buthalitone and 27.8 minutes for thiopentone.

O'Mullane (1957) has reported that, in a preliminary trial with an unspecified number of cases, an average dose of 50 mg/stone (6.3 kg) body weight of buthalitone was equivalent to an average dose of 25 mg/stone body weight of thiopentone. On the other hand, reporting on the e.e.g. changes produced in three volunteers, he found that 75 mg/stone body weight of buthalitone and 25 mg/stone body weight of thiopentone produced comparable depths of anaesthesia as assessed by the method of Kiersey et al. (1951).

Another two comparisons using volunteers have been carried out by Wyant, Dobkin and Aasheim (1957), when seven agents were compared in five subjects, and Dobkin and Wyant (1957), when the same seven agents were compared in seven subjects. The results as regards buthalitone and thiopentone in the first paper were that an average dose of 94.9 mg per stone body weight (14.8 mg/kg body weight) of the former was followed by an average recovery period of 7 minutes whilst the average dose of the latter, 67.3 mg per stone body weight (10.5 mg/kg body weight), produced an average recovery time of 30 minutes. In the second paper, using the same dosage with each drug, viz. 500 mg per square metre of body surface area, buthalitone produced an average of 5 minutes sleep while thiopentone produced an average of 34 minutes sleep.

Keéri-Szántó and Labarre (1957) report on a series of 37 cases of uterine curettage using buthalitone in intermittant dosage. These were compared with a similar series of 24 cases using intermittent dosage of thiopentone. The total amounts of the drug used averaged 71.4 mg per stone body weight (11.2 mg/kg body weight) for buthalitone and 44.8 mg per stone body weight (7.0 mg/kg body weight) for thiopentone.

Murray (1957) has reported upon a clinical trial of buthalitone in 850 cases. A comparison with thiopentone was made in 40 females aged between 16 and 46 years who were undergoing uterine curettage. The dose of each drug was recorded as the average dose per kg body weight per minute. This dose was found to be 2.8 mg for the 20 patients receiving buthalitone and 1.5 mg for those receiving thiopentone.

The only comparison of buthalitone and thiopentone solely in outpatient anaesthesia is that of Simmons and Blanshard (1957). These workers reported upon a trial in 208 patients, the majority of whom were unpremedicated. The minority who received premedication were given only 0.65 mg atropine. The drugs were given by two techniques: a single dose technique with no supplementation, and a technique involving the use of the thiobarbiturate in intermittent dosage and supplementing it by the administration of nitrous oxide with 20 per cent oxygen. Two dosage rates were used. Initially (Trial Period 1), the dose used was the minimum required to produce hypnosis throughout the operation. Trial Period 2 involved the use of a dosage of thiobarbiturate which produced satisfactory operating conditions. The criteria for recovery were a co-ordinated response to a painful stimulus, verbal accessibility and ability to sit up, and the time of reaching each of these stages was measured. The average dosages of buthalitone and thiopentone used were 5.72 and 4.23 mg per lb. body weight (12.58 and 9.30 mg/kg body weight) respectively in Trial Period 1, and 8.19 and 3.93 mg per lb. body weight (18.01 and 8.64 mg/kg body weight) respectively in Trial Period 2. The results showed a considerable increase of recovery time with thiopentone as compared with buthalitone in Trial Period 1. This increase was much less in Trial Period 2 and was not statistically significant. A high incidence of vomiting, coughing and hiccup with buthalitone and a high incidence of coughing with thiopentone was reported.

METHOD

In our previous investigation (Henderson and Mackett, 1957), all patients received a single induction dose of buthalitone at the rate of 70 mg per stone body weight (10.9 mg/kg body weight) and anaesthesia was maintained with nitrous oxide 8 litres per minute and oxygen 2 litres per minute. In the present investigation, 100 consecutive cases from the first series were compared with four series, each of 100 cases, having thiopentone as the inducing agent. The dosage

rates per stone body weight in the four thiopentone series were 25 mg, 30 mg, 35 mg and 40 mg (3.9 mg, 4.7mg, 5.4 mg and 6.2 mg/kg body weight). Initially, after some trial cases, it was felt that a dosage of 25 mg per stone would be roughly equivalent to our previous rate of 70 mg per stone of buthalitone as regards operating conditions and recovery times. Having completed the series at that dosage, we found that the incidence of movements of the patients was greater than that occurring in the buthalitone series (table II). This suggested that, in some respects, the dosage was too low and it was increased to 30, 35 and 40 mg per stone in subsequent series in order to try to obtain a series in which the incidence of movements was comparable to that of the buthalitone series.

As before, the "waking", "sitting" and "standing" times were observed. These were recorded to the nearest half-minute and were measured from the conclusion of the anaesthesia. The waking time was that at which the patient was sufficiently awake to answer simple questions. The sitting time was when the patient could sit up unaided and the standing time was when he or she could stand and walk unaided.

Records were also made of the incidence of movements, vomiting, cough, hiccup and laryngeal spasm. Movements were classified as "slight" when they caused no interference with the operation; "moderate" when, with a moderate degree of restraint, the operation could be continued satisfactorily; and "severe" when the operating had to be interrupted so that the patient could be quietened.

In 40 cases (20 with each drug, selected at random) electrocardiograms were performed to see whether there was any toxic effect on the myocardium with the doses used in the present series and, if so, whether there was any difference in the incidence of electrocardiographic changes between the two drugs.

In order to exclude as many variable factors as possible in the five series, all patients had the same premedication of atropine (0.64 mg) half an hour before operation. A 10 ml all-glass syringe fitted with a size 12 needle was used and the injections of the thiobarbiturate were given as rapidly as possible. Buthalitone was used in a 10 per cent solution and thiopentone in a 5 per cent solution so that the volumes of solution injected were as nearly as possible the same. All injections were given and all observations made by the same person.

RESULTS AND DISCUSSION

The recovery times are shown in table I and the incidence of movements during operation in table II.

The first thiopentone series to be completed was that using a dosage of 25 mg per stone (6.3 kg) body weight. Although this rate of dosage was found to give average recovery times only slightly longer than those of the series receiving buthali-

TABLE I
Recovery Times

	Buthalitone	Thiopentone			
Dose per stone (6.3 kg) body weight	70 mg	25 mg	30 mg	35 mg	40 mg
Duration of anaesthesia					
Average (min)	7.29	8.42	7.97	11.71	10.56
Limits (min)	1–40	1–22	1–23	3–59	1–27
Waking time					
Average (min)	1.36	1.45	1.53	1.81	3.39
Limits (min)	½–8	½–7	½–5	½–6½	1–23½
Sitting time					
Average (min)	2.30	2.53	2.62	2.75	4.94
Limits (min)	1–15	1–21	1–12½	1–7½	1½–29½
Standing time					
Average (min)	11.70	14.67	13.54	12.98	23.24
Limits (min)	2–40	1½–46	2½–36	1½–48	3½–65½

TABLE II
Incidence of Movements During Anaesthesia.

	Buthalitone	Thiopentone			
Dose per stone (6.3 kg) body weight	70 mg	25 mg	30 mg	35 mg	40 mg
Slight movements	9	14	7	7	6
Moderate movements	2	8	7	6	1
Severe movements	–	7	2	–	–
Total of movements requiring restraint	2	15	9	6	1

tone at the rate of 70 mg per stone body weight, the incidence of movements requiring restraint was 15 per cent as compared with 2 per cent of the cases receiving buthalitone. Similarly, in the series receiving 30 mg per stone body weight of thiopentone, the incidence of movements requiring restraint (9 per cent) was again greater than that of the buthalitone series and there was slight prolongation of the recovery times. These results were taken as an indication that, although the average durations of anaesthesia in the thiopentone series were longer than those in the buthalitone series, the depth of anaesthesia produced by the thiopentone was less than that of the buthalitone. On the other hand, the two series receiving 35 and 40 mg per stone body weight of thiopentone had an incidence of movements requiring restraint more nearly comparable with that of the buthalitone series. However, in the series receiving 40 mg per stone body weight, the average recovery times were considerably prolonged. These results would suggest that, with this dosage, some degree of saturation of the body fat depots probably occurs.

In comparing these results, we first had to determine whether there was any correlation between the duration of anaesthesia and the recovery (standing) time for each series. This was done and the correlation coefficient, r, was examined for significance by the t-test in each series. The results of this are shown in table III. With 98 (100 – 2) d.f., the significant value of the correlation coefficient at the 5 per cent level is 0.195. It will therefore be seen that only the coefficients for the buthalitone and the 25 mg thiopentone series are significant at the 5 per cent level and that their value decreases with increasing dosage of thiopentone. This suggests that, with a small dose of thiopentone or buthalitone, when the duration of anaesthesia is prolonged the recovery time is influenced more by the effects of the nitrous oxide than those of the thiobarbiturate. On the other hand, the negative correlation coefficient with the 40 mg per stone thiopentone series indicates that there is a tendency for a longer anaesthesia to be followed by a shorter recovery time. This can be explained on the supposition that, in those cases of short duration, the patient had still to recover from the effects of the thiopentone when the nitrous oxide administration had been stopped. Conversely, the effects of the thiopentone would be less after longer anaesthesia and recovery would be mainly from the effects of nitrous oxide anaesthesia.

TABLE III
Table of Correlation Coefficients between Duration of Anaesthesia and Standing Times (100 cases in each series).

	Dose mg per stone (6.3 kg) body weight	Average duration min	Average standing time min	Correlation coefficient, r
Buthalitone	70	7.29	11.70	0.24
Thiopentone	25	8.42	14.67	0.31
	30	7.97	13.54	0.08
	35	11.71	12.98	0.11
	40	10.56	23.24	−0.14

In view of these findings, it was felt that the comparison between the various doses of thiopentone and the buthalitone should be limited to those cases with a shorter duration of anaesthesia in order to limit as far as possible one variable factor. In the preliminary calculations, each series was split up into a group having a duration of up to 10 minutes and another comprising cases with a duration of 10½ to 20 minutes. However, in each series, there was no significant difference between the two groups and so the final comparison is based on the results of cases where the duration of anaesthesia did not exceed 20 minutes. These figures are shown in table IV.

When these corrected average standing times of the thiopentone series are compared with that of the buthalitone series, only the differences between thiopentone 25 and 40 mg per stone and buthalitone are significant at the 5 per cent level when examined by the *t*-test (see table V).

The relationship between the recovery times for buthalitone and the thiopentone 25 mg per stone series may be explained by the fact that the thiopentone series has a longer average duration of anaesthesia than the buthalitone series and, with this dosage of thiopentone, both have a positive correlation between duration of anaesthesia and recovery time. In the case of the thiopentone 40 mg per stone series, it can probably be assumed that, in most of the patients, a partial saturation of the body fat with thiopentone has occurred.

If we now consider the incidence of movements during anaesthesia (table II), we find that, with a dosage of thiopentone of 25 mg per stone body weight, there is an incidence of 18 per cent above that for buthalitone. Using the χ^2 test, this is shown to be significant ($0.01>p>0.001$). This was also true of the incidence of moderate and severe movements only (movements requiring

TABLE IV

Recovery Times of Cases where the Duration of Anaesthesia did not Exceed 20 minutes.

	Buthalitone	Thiopentone			
Dose per stone (6.3 kg) body weight	70 mg	25 mg	30 mg	35 mg	40 mg
Number of cases	95	99	97	92	95
Average duration of anaesthesia (min)	6.32	8.32	7.47	9.41	9.89
Waking time					
Average (min)	1.35	1.44	1.52	1.72	3.40
Limits (min)	½–8	½–7	½–5	½–6½	1–23½
Sitting time					
Average (min)	2.27	2.54	2.57	2.65	4.95
Limits (min)	1–15	1–21	1–12½	1–7½	1½–29½
Standing time					
Average (min)	11.32	14.50	13.21	13.21	23.80
Limits (min)	2–35	1½–46	2½–33½	1½–48	3½–65½

TABLE V

The Significance of the Differences between the various Average Standing Times of the Thiopentone Series compared with that of the Buthalitone Series.

Buthalitone 70 mg per stone (6.3 kg) average standing time (min)	Thiopentone: Dose mg per stone (6.3 kg)	Thiopentone: Average standing time (min)	*t*	*p*	
11.32	25	14.5	2.74 ($v=192$)	0.01	Significant
	30	13.21	0.55 ($v=190$)	>0.50	Not significant
	35	13.21	0.48 ($v=185$)	>0.50	Not significant
	40	23.8	7.84 ($v=188$)	0.001	Significant

restraint) ($0.001>p>0.0001$). The incidence of movements requiring restraint in the 30 mg per stone thiopentone series was compared with that of the buthalitone series and was also found to be significantly increased ($0.05>p>0.02$). In all other cases there was no significant variation in the incidence of total movements and of movements requiring restraint.

These results of the differences in standing times and the incidence of movements requiring restraint taken together suggest that the series receiving 35 mg per stone body weight of thiopentone most nearly compares with that receiving 70 mg per stone body weight of buthalitone. Thus in the 25 mg and 30 mg per stone thiopentone series, there is a significantly increased incidence of movements requiring restraint suggesting that the degree of anaesthesia is less than that attained with the buthalitone, while the greatly increased recovery time of the 40 mg per stone thiopentone series shows that the depth of anaesthesia is probably greater than that of the buthalitone series.

Table VI shows the comparable rates of dosage in seven other published series comparing buthalitone with thiopentone. Our ratio of 1:2 of thiopentone to buthalitone is closely comparable to four of these seven series. In view of this fact, we feel that this method of assessing equipotent anaesthetic dosages could be employed usefully as a means of standardizing the potency of other thiobarbiturates and intravenous anaesthetic agents.

Table VII shows the incidence of other side-effects during and after anaesthesia. Vomiting occurred in 7 per cent of cases receiving buthalitone and in 11 per cent of the cases having 35 mg per stone body weight of thiopentone. Using the χ^2 test, this difference and the differences between the other series were found to be statistically not significant. Two cases of laryngeal spasm occurred; one in each of the series with the higher dosages of thiopentone.

Influence of Sex.

Dundee (1954) has investigated the influence of various factors, including sex, upon the dosage of thiopentone. He found that males, on the

TABLE VI

Table of Comparative Potencies in Published Series.

Authors	Year	Dosage of thiopentone (mg)	Dosage of buthalitone (mg)	Ratio
Freuchen	1956	8.3	15.1	1:1.8
O'Mullane (clinical) (e.e.g.)	1957	25	50	1:2
		25	75	1:3
Keéri-Szántó and Labarre	1957	44.8	71.4	1:1.6
Murray	1957	1.5	2.8	1:1.8
Simmons and Blanshard	1957			
(Trial period 1)		4.23	5.72	1:1.3
(Trial period 2)		3.93	8.19	1:2.1
Henderson and Mackett	1958	35	70	1:2

TABLE VII

Incidence of Side-effects.

	Buthalitone	Thiopentone			
Dose per stone (6.3 kg) body weight	70 mg	25 mg	30 mg	35 mg	40 mg
Cough	3	3	1	6	3
Hiccup	2	–	–	3	5
Vomiting	7	13	7	11	12
Laryngeal spasm	–	–	–	1	1

average, require more thiopentone than females. Vollmer and Haaf (1954) have had similar results with buthalitone. As both sexes in our series were given the thiopentone and buthalitone at the same rate of dosage, we decided to analyze our figures and the results of this are shown in table VIII.

If the corrected rates for the standing times are taken (where the duration of anaesthesia does not exceed 20 minutes) then in all the series except that receiving 25 mg per stone of thiopentone there is a significant increase in the standing times of female cases when compared with the corresponding male cases, the values of t varying from 1.97 to 2.72, which are all significant at the 5 per cent level.

If the results of each thiopentone series are broken down according to the sexes and these are then compared with the corresponding sex of the buthalitone series, it is found that the only male series which is not significantly different from the buthalitone series is that receiving 35 mg per stone of thiopentone. In the case of the female series, the only one significantly different from the buthalitone series is that receiving 40 mg per stone of thiopentone. Thus, once again, the 35 mg thiopentone series would appear to compare most closely with the 70 mg buthalitone series.

Electrocardiographic Changes.

Although a high incidence of electrocardiographic abnormalities has been noted following the administration of thiopentone to experimental animals (Gruber et al., 1938; Kohn and Lederer, 1938; Widenhorn et al., 1938; Gruber, 1937, 1941), the results in man have been variable.

Volpitto and Marangoni (1938) reported on the abnormalities produced by thiopentone, hexobarbitone and thioethamyl. Of 11 administrations of thiopentone, there was slight tachycardia but no abnormalities of the QRS complex or of the PR interval. This absence of abnormalities was also noted by Rosner et al. (1953) who found none related to thiopentone alone but noted depression of ST and decreased voltage of T wave in the presence of hypopnoea. On the other hand, Carraway (1939) noted electrocardiographic changes in 22 out of 52 cases having thiopentone; Burstein et al. (1950), 1 case out of 5; Stephen et al. (1953) who noted 37 instances of changes out of 238 cases when recordings were made immediately after induction with thiamylal, thiopentone and hexobarbitone; and Rollason and Hough (1958) who make a detailed report of the changes seen in 52 patients following induction with thiopentone.

Johnstone (1951), using a fixed dosage of 500 mg of thiopentone in a series of 100 cases, has noted an increase of sinus rate in patients who had no premedication and a decrease in rate in those who had 1.3 mg of atropine 20 minutes before induction. He also observed occasional decrease in voltage of P waves and of T waves.

Little work appears to have been done upon the electrocardiographic changes produced by

TABLE VIII

The Influence of Sex upon the Recovery Times: Corrected Results (duration of anaesthesia not exceeding 20 minutes).

		Males				Females				Total			
	Dose mg per stone (6.3 kg) body weight	No. of cases	Waking time (min)	Sitting time (min)	Standing time (min)	No. of cases	Waking time (min)	Sitting time (min)	Standing time (min)	No. of cases	Waking time (min)	Sitting time (min)	Standing time (min)
Buthalitone	70	54	1.40	2.17	9.79	41	1.28	2.46	13.43	95	1.35	2.27	11.32
Thiopentone	25	69	1.39	2.46	13.07	30	1.57	2.73	16.40	99	1.44	2.54	14.50
	30	57	1.58	2.57	12.02	40	1.54	2.55	14.91	97	1.52	2.57	13.21
	35	56	1.75	2.68	11.69	36	1.78	2.76	15.97	92	1.72	2.56	13.21
	40	63	3.11	4.50	21.07	32	3.98	5.84	28.86	95	3.40	4.95	23.80

buthalitone in man, but Weese and Koss (1954) report that no irregularities were observed in their experiments with dogs.

Our technique for making the recordings was as follows. When the patient was lying on the table and the leads had been attached, a control tracing of leads I, II and III was made. A continuous tracing of lead II was made during the injection of the thiobarbiturate and this was continued for 30 seconds after the start of the injection. The facemask was then applied and the nitrous oxide and oxygen mixture administered. Tracings of leads I, II and III were then made at 1 and 5 minutes after the start of the injection. Recordings of these three leads were continued at 5 minute intervals throughout the operation. A final tracing of leads I, II and III was made shortly after the "waking time" had been observed.

TABLE IX
Incidence of Electrocardiographic Abnormalities.

	Buthalitone	Thiopentone
Total number of cases	20	20
Tachycardia	9	9
Extrasystoles	–	3
Prolongation of QT interval	20	20

The results are shown in table IX. Sinus tachycardia (of 20/min or more) was seen frequently (9 cases with each drug) during and just after injection, but it was always transient. Occasional ventricular extrasystoles occurred shortly after injection in 3 patients receiving thiopentone; none were produced by buthalitone. The QT interval was prolonged in every case with both drugs. No abnormality of the PR interval, QRS complex or T wave was observed in any case.

SUMMARY

A short review of buthalitone sodium and the methods by which it has been compared with thiopentone is given.

A series of 100 cases receiving buthalitone has been compared with four series, each of 100 cases, given thiopentone in differing dosage rates.

By the technique described, buthalitone was found to require approximately twice the dose to produce an anaesthetic effect equivalent to that of thiopentone. This result has been compared with comparative studies by other workers. When buthalitone is used in twice the dosage of thiopentone, no significant difference in recovery times or side-effects between the two drugs was found.

It is suggested that the method described may be a useful means of comparing the potency of thiobarbiturates and other intravenous anaesthetic agents.

The incidence of electrocardiographic abnormalities in 20 random cases with each drug is reported.

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MINOR LARYNGEAL SEQUELAE OF ENDOTRACHEAL INTUBATION

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THE laryngeal complications of endotracheal anaesthesia may be divided into major and minor groups. Although major complications are not common, reports of laryngeal and tracheal lesions of various types do appear fairly regularly in the literature. On the other hand, minor sequelae of intubation figure but briefly. It has been possible to find only four reported series, none of which is large and the latest of which was contributed in 1951. In view of this, it seemed worthwhile to investigate the subject in a fairly large number of cases.

In order to give a more complete picture of intubation sequelae both the major and minor disorders mentioned in the literature will be described before discussing the present investigation and results.

MAJOR COMPLICATIONS

The most commonly reported laryngeal complication following intubation is granuloma formation. A report of five cases was given by Griffiths (1932) and since then case reports have appeared with great regularity in laryngological and anaesthetic journals all over the world.

Jackson (1953) reviewed the occurrence of this condition and discussed the aetiological factors. It should not be thought that this condition is purely a postintubation phenomenon. Of 293 cases reported by Jackson and Jackson prior to 1935, none were sequelae of intubation. Of 48 cases recorded by Norris between 1948 and 1952, only 6 followed intubation. However, 55 cases were reported in Britain between 1932 and 1954. The site of the granuloma is usually at the tip of the vocal processes of the arytenoid cartilages. The reasons for this localization advanced by Jackson are the following:

(1) There is a very thin mucoperichondrial covering at this area.
(2) There is incessant movement of the arytenoids.
(3) There is a hammering together of these cartilaginous points.

If anaesthesia and intubation is performed, to these general factors may be added any or all of the following:

(1) Clamping of the cords on to the tube on intubation, and again if anaesthesia lightens.
(2) Hooking of the arytenoid by the open end of the tube.
(3) Roughness of the tube itself if any is present.

The sequence of events is that ulceration follows the original trauma whatever the mechanics of this trauma may be. This ulcer is not allowed to heal, due to incessant movement of the cords, and granuloma formation follows. If the condition is diagnosed at the ulcer stage, then, enforced and complete silence may interrupt this sequence and promote cure. If granuloma formation does occur, surgical treatment may be required.

Young and Stewart (1953) point out that as a sequel to intubation, contact ulcer is commoner in the female, whereas as a spontaneously occurring condition it is commoner in the male. They further call attention to an article by Dwyer, Kronenberg and Saklad (1949) in which they suggest that the curve of an endotracheal tube is such as to cause pressure on the front wall of the trachea and against the base of the glottis. The symptomatology which they quote is hoarseness from the time of operation, possible intermittent loss of voice, dyspnoea, pain or discomfort and very rarely haemoptysis. They stress that resting

the voice may produce a cure at an early stage, but also point out that the granuloma may disappear spontaneously without requiring surgical intervention. A case report by Melick, Urry and McAdams (1954) includes a histological report of a postintubation granuloma removed surgically. This was "an active growth of vascular granulation tissue". In an analysis of 35 cases, Howland and Lewis (1956) point out that the position of the head would appear to be an important aetiological factor. Thus, 21 of these cases followed thyroid operations with the head extended beyond the neutral position, and in one the patient was prone with the head rotated. They again point out the greater frequency of the condition in the female and suggest that this may be due to the following factors: (*a*) The larynx of the female is smaller; (*b*) the mucosa on the true cords is thinner; (*c*) the incidence of thyroidectomy is higher.

Epstein and Winston (1957) could show no relationship between the occurrence of granuloma and either time of operation or difficulty in intubation. They stress that pressure of the tube against the vocal processes is probably the main causative factor, especially where the neck is excessively flexed with the tube in situ.

Another complication reported is that of subglottic membrane. Three cases are reported by Etsten and Mahler (1951). In none of these cases was there any difficulty in intubation although the tubes gave a very snug fit. The postoperative sequences were all similar. There was hoarseness followed by tachypnoea and stridor 24–48 hours postoperatively. Bronchoscopy revealed a normal epiglottis and larynx, but in the subglottic region a membrane was found, the removal of which led to alleviation of symptoms. A recurrence of symptoms followed by bronchoscopic removal of another piece of membrane gave final cure.

The aetiology suggested is that pressure from the tube led to injury followed by leucocytic accumulation, degeneration of cells and membrane formation.

Two somewhat similar cases are reported in children by Haines and Powell (1955). Intubation, however, was difficult in these cases, the tubes being arrested at the level of the cricoid. Tracheotomy was needed due to intense oedema in the subglottic tissues. One of these cases, although showing marked improvement after tracheotomy, died suddenly 38 hours postoperatively. The postmortem showed "a white sloughing ring encircling the airway and somewhat obstructing it". This was immediately below the vocal cords.

Ransom (1947) reported a case of fatal tracheitis following intubation. At this time, the endotracheal tubes were sterilized by washing them in biniodide of mercury, and in this case it was suggested that this had not been properly removed.

Perhaps the most unusual complication reported is of a fatality following rupture of the cuff of an endotracheal tube. In this case, reported by Lennon and Rovenstine (1939) a loud noise like an explosion was heard during operation, and as the circuit was found to be no longer completely closed it was realized that the cuff had ruptured. The patient's condition deteriorated and at the end of the operation fresh blood was found in the endotracheal tube and in the trachea itself. The patient survived only a few hours and at a postmortem, among the findings, was a rupture through all the layers of the trachea.

Belam and Zuck (1953) report a postmortem finding of pressure necrosis of the laryngeal mucosa following the use of a cuffed tube, in a very ill patient who had, at times, a systolic blood pressure below 50 mm Hg. Following this case they measured pressures in the cuff and reported readings varying between 120 and 180 mm Hg. Adriani and Phillips (1957) investigating the use of a cuff on the endotracheal tube also measured intra-cuff pressures and reported values from 90 to 200 mm Hg. They pointed out that even with those pressures, when the pressure in the rebreathing bag was 15–20 mm Hg, the actual pressure on the laryngeal wall was 10–15 mm Hg. They showed that a pressure of over 1000 mm Hg was necessary to rupture a cuff, and when this was done experimentally in dogs no harm resulted. They further pointed out that a cuff afforded complete protection against aspiration into the trachea, whereas a throat pack was much less reliable.

Miscellaneous complications reported by Flagg (1951) include haemorrhage of vocal cords, oedema of cords, larynx or trachea, paralysis of vocal cords, tracheal webs, perforation of the

trachea and even perforation of the oesophagus by a protruding stilette used during intubation.

On the question of duration of intubation, many cases of prolonged intubation are recorded. Gillespie (1942) reported a case intubated for 51 hours, with only temporary ill effects. Dwyer, Kronenberg and Saklad (1949) reported on cases examined either by bronchoscopy or at autopsy. Traumatized, congested areas always appeared within 2–4 hours, but actual ulceration of the tracheal mucosa was never seen following less than 6 hours intubation. Longer periods of intubation—up to 15½ hours—showed areas of ulceration. These areas overlaid the tracheal cartilages. The rest of the mucosa of the larynx and trachea showed diffuse oedema.

MINOR COMPLICATIONS

Kaye (1936) gave an analysis of 518 case records. There was no direct questioning of patients regarding their throats in this series and no details are given regarding the ease of intubation or the time of operation. Thus, only patients who had complained and whose complaints had been noted, were included. Of 326 patients in whom wide bore endotracheal tubes were used, 1 complained of hoarseness without pain, 5 had definite laryngitis or tracheitis, and 4 had pharyngeal ulceration. Of the remaining 192 patients in whom an insufflation technique through a narrow tube was used, 1 had hoarseness and 1 laryngitis or tracheitis.

Donnelly, Grossman and Grem (1948), in an article describing the possible lesions which may occur due to intubation, also describe postoperative laryngoscopic examination of 100 cases, 99 by mirror and 1 by autopsy. In these cases, most of the intubations were performed by first-year residents. The lubricant was 5 per cent Intracaine and the anaesthetist noted whether he thought the intubation was traumatic or atraumatic; 83 were oral intubations and 17 nasal; time varied from 30 minutes to 22 hours; 38 intubations were labelled traumatic and 62 atraumatic. On laryngoscopy, 60 cases had a lesion of some sort, 39 had no lesion and the 100th case had no lesion at autopsy. The lesions were of varying type, 44 being intralaryngeal and 19 extralaryngeal, some cases having more than one type.

Although this appeared to be a large number of injuries, in the main they were mild and relatively symptomless. No details of the number of actual complaints from patients are given. As part of their conclusions, they state:

"As shown in our series, even with residents recently introduced to the endotracheal technique, only relatively minor traumatic effects were sustained."

"The advantages of endotracheal anaesthesia which have not been discussed in this paper, far outweigh any minor undesirable effects discovered in this study."

Wylie (1950) discussed 150 cases re-examined by direct laryngoscopy at the end of the operation. Of these, 100 cases had been intubated with a Magill laryngoscope and 47 showed evidence of trauma. 57 cases complained of mild sore throat and 13 of severe sore throat. Of the 47 cases showing signs of trauma, 31 had a mild sore throat, 10 had a severe sore throat and 6 no sore throat. This leaves 26 cases of mild sore throat and 3 of severe sore throat who showed no evidence of trauma.

Of 50 cases intubated with a Macintosh laryngoscope, 18 showed signs of trauma and there were 23 complaints of sore throat.

No information is given regarding difficulty in intubation or length of operation. In this series, then, 46 per cent of cases intubated with a Macintosh and 70 per cent of cases intubated with a Magill laryngoscope had some degree of sore throat.

In 1951 Baron and Kohlmoos reported on 80 cases on whom laryngoscopy was carried out postoperatively. All had mild sore throats lasting 24 hours and 3 had severe sore throats lasting 48–72 hours; 50 cases were hoarse; 34 of these showed redness of the vocal cords and 16 had normal cords.

PRESENT INVESTIGATION

The purpose of the present investigation was to assess the number of minor laryngeal sequelae produced by intubation in the everyday anaesthetic practice of a fairly large teaching hospital. It was not, in any way, an attempt to observe the best method or route of intubation or the best drugs to use for the purpose. No anaesthetist

was asked to depart from his normal practice, regarding which cases to intubate or how to perform this manoeuvre. Anaesthetists of all grades from Senior House Officer to Consultant took part.

The ordinary anaesthetic record completed by the anaesthetist in the Western Infirmary gives information regarding route of intubation, the presence or absence of a cuff on the tube or of a pack in the mouth and the position of the patient. The only additional information required was the degree of difficulty, if any, experienced in intubation, the duration of the intubation, the lubricant used and the presence or absence of a Ryle's or oesophageal tube. In order to standardize the ideas of ease or difficulty in intubation, the following grades were described:

(1) *Easy.* A good view of the larynx was obtained. The cords were either open or yielded to slight pressure with the tube. Only one attempt was needed. This was signified with an "X".

(2) *Slight difficulty.* The cords were closed and did not yield to slight pressure. A waiting period was necessary but no more than two attempts were needed to pass the tube. This was signified with an "XX".

(3) *Any more difficulty than the above.* Signified "XXX".

Time of intubation was recorded as more or less than 1 hour.

The lubricants used were Lubafax or 5 per cent lignocaine in a water soluble base.

In the Western Infirmary it is taught that the largest tube which can be passed comfortably is the correct tube, and that if a cuff is to be inflated it is done by the method of Guedel and Waters (1931). It was assumed, therefore, that these criteria were observed for all cases. The great majority of cases were intubated using a Macintosh larnygoscope.

It was originally intended that all the patients should be interviewed on the 2nd or 3rd postoperative day, so that the patient would have recovered from the immediate effects of the operation, and also in the hope that any sore throat which appeared immediately postoperatively would have had time to resolve. The hope proved forlorn, in that some of the sore throats lasted more than 2–3 days, thus necessitating a second visit, and the intention became impracticable due to the demands of ordinary commitments.

Finally, one day each week was set aside to interview the cases, so that they were seen at some time between the 2nd and 8th postoperative days.

When interviewed, the following questions were asked:

(1) Did you have a sore throat after your operation?

If the answer was "yes" then they were asked if it was very sore or just slightly sore, how long it had lasted, and whether or not they had notified anyone. They were also asked if they were liable to sore throats normally. If the answer was "no" then they were asked:

(2) Did you have even a slight tickle in the back of your throat or was it painful to swallow?

(3) Did you have any pain in the chest? When this was asked the sternal area was indicated with a finger.

If the patients seemed perturbed about the questioning, or even if they seemed interested, then it was explained that a few people complained of sore throat postoperatively and this was just a check-up to see how many there were.

Most patients were very definite in their answers, either "yes" or "no." A few said they did not remember and they were classified as negative. A few, when pressed, admitted to a slight tickle in the throat and although it may well be that they were merely being obliging, they were classified as positive.

Patients with oesophageal tubes in situ during or after operation were not included: nor were any intra-oral operations or thyroid operations. A number of cases who were not intubated (100) were also interviewed to act as a control.

The results of the present series are shown in tables I–XI.

It will be seen that in table II the total number of complications is 115. This is because the 4 patients who suffered both sore throats and hoarseness, are included under those headings separately, as well as under the combined heading.

The first three tables show merely the overall figures. The next series of tables present an attempt to relate the incidence of complications to the various factors involved.

TABLE I

No. of patients interrogated	No. with complications	Percentage with complications
521	111	21.3

TABLE II

Slight sore throat	Percentage of total cases	Severe sore throat	Percentage of total cases	Hoarse	Percentage of total cases	Lost voice	Percentage of total cases	Sore throat and hoarse	Percentage of total cases
83	15.9	13	2.5	17	3.3	2	0.4	4	0.8

TABLE III

No. of cases	Easy intubation	Percentage of total cases	Difficult intubation	Percentage of total cases	Very difficult intubation	Percentage of total cases
521	447	85.8	57	10.9	17	3.3

TABLE IV

No. of females	No. of complications	Percentage	No. of males	No. of complications	Percentage
279	75	26.9	242	36	14.9

TABLE V

No. of cases intubated with cuffed tube	No. of complications	Percentage	No. of cases intubated with non-cuffed tube	No. of complications	Percentage
378	82	21.7	143	29	20.3

TABLE VI

No. of cases using lignocaine as lubricant	No. of complications	Percentage	No. of cases using Lubafax as lubricant	No. of complications	Percentage
374	80	21.1	147	31	21.0

TABLE VII

No. of cases lasting more than 1 hour	No. of complications	Percentage	No. of cases lasting less than 1 hour	No. of complications	Percentage
187	37	19.8	281	69	21.0

The total number of cases does not amount to 521. This was because some of the records were not completed for this factor.

TABLE VIII

No. of cases of easy intubation	No. of complications	Percentage
447	99	22.1
No. of cases of difficult intubation	**No. of complications**	**Percentage**
57	10	17.5
No. of cases of very difficult intubation	**No. of complications**	**Percentage**
17	2	11.5

incidence in Wylie's series, where a Macintosh laryngoscope has been used, and 70 per cent where a Magill laryngoscope has been used, and very much less than the 100 per cent incidence of mild sore throat reported by Baron and Kohlmoos.

Difficulty in intubating did not appear to affect the incidence of sore throat adversely. This may be due to the fact that the conditions laid down were fairly stringent or else to the fact that they only covered the actual introduction of the tube into the larynx and not the amount of force used during the actual laryngoscopy. All the cases in this series, except one, were intubated with the aid of a relaxant and it may be that the ease

TABLE IX

Position of patient	No. of cases	No. of complications	Percentage
Supine, Trendelenburg, Lithotomy	445	91	20.2
Prone	34	10	26.5
Lateral	38	8	21.0
Sitting up	1	1	100.0
Knee-elbow	3	1	33.3

TABLE X

No. of complications	No. notified	Percentage	No. not notified	Percentage
111	51	46	60	54

TABLE XI

No. of cases	No. with complications lasting less than 2 days	Percentage of total cases	No. with complications lasting more than 2 days	Percentage of total cases
521	57	10.9	54	10.3

DISCUSSION

The results of this series do not show any great similarity to those previously published. Thus in Kaye's series there is a 3.2 per cent incidence of actual complaints reported in case records, whereas in this series there is a 10 per cent incidence of complaints to nursing or resident staff. How many of these would have actually been noted in case records is difficult to estimate.

The 21.3 per cent of complaints elicited by interrogation is much less than the 46 per cent afforded by these drugs has helped to reduce the sore throats, due to actual trauma around the mouth and throat, leaving only the incidence due to the presence of a foreign body in the larynx and trachea.

Consideration of the various factors involved shows a markedly higher incidence of complications in the female than in the male. Statistically this difference is highly significant and agrees with the findings regarding granulomata already quoted. It is worth noting, however, that this

series does not include any thyroid operations and the vast majority of the cases had the head in the neutral position. The higher incidence of thyroidectomy in the female cannot therefore be advanced as the explanation for the higher incidence of sore throat in this series.

The presence or absence of a cuff on the tube, the lubricant and the time of operation appeared to make no significant difference to the incidence of complications.

On the subject of position a higher incidence is found in the prone position than in the supine, lithotomy, Trendelenburg or lateral positions. Statistically this is not a significant figure due to the small number of cases involved. It might merely be termed mildly suggestive. The number of cases in the knee-elbow and sitting-up positions is much too small to have any significance.

In the control series of 100 cases, only 2 had mild sore throats lasting 12 hours. Of those, 1 was subject to sore throats normally.

SUMMARY

521 cases have been interrogated concerning the incidence of postintubation throat complications: 15.9 per cent had a slight sore throat; 2.5 per cent had a severe sore throat; 3.3 per cent were hoarse; 0.4 per cent lost their voices, and 0.8 per cent had sore throats and were also hoarse; 10.3 per cent had complications lasting 2 or more days, and 10.9 per cent had complications lasting less than 2 days. The complications lasted from 3 hours to 7 days.

The incidence was affected only by the sex of the patient, being much greater in the female. There was a greater incidence also in the prone position but the figures were not statistically significant.

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HALOTHANE ("FLUOTHANE") IN A COUNTRY HOSPITAL

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REPORTS on the extensive clinical trials of halothane carried out by Johnstone (1956), Bryce-Smith and O'Brien (1956), and Brennan, Hunter and Johnstone (1957) will have been studied with great interest by most anaesthetists. Many, like the writers, must have wondered whether the new discovery could bring about a basic change in current anaesthetic practice.

For more than ten years some variant of balanced anaesthesia has been used in most anaesthetic rooms. The aim has been to produce a flaccid narcosis less harmful to the patient than the toxic depths of chloroform and ether anaesthesia.

The pioneers of halothane proved to their own satisfaction that a deep narcosis free from toxic after-effects, explosion risks and cardiac catastrophe could be obtained with this drug. We decided in July 1957 to attempt to duplicate their results in the theatres of the North Down Hospitals Group.

This group includes Ards Hospital (320 beds) a busy general hospital with the usual departments including a 36 bed maternity unit, and Bangor Hospital, a converted cottage hospital of 40 beds, where intermediate and minor surgery, gynaecology, otolaryngological surgery and casualty work are carried out. This Hospital Group is self

TABLE I

Classification of operations under halothane anaesthesia

General surgery		*Gynaecology*	
Gastrectomy	4	Hysterectomy	33
Gastro-enterostomy	1	Pelvic floor repairs	49
Cholecystectomy	12	Wertheim's hysterectomy	3
Hemicolectomy	3	Laparotomy	21
Laparotomy	19	Caesarean section	16
Perforated viscus	10	Vulvectomy	1
Colostomy	8	D. and C.	165
Short circuits	5		288
Appendicectomy	124	*Genito-urinary*	
Hernia repair	22	Prostatectomy	18
Strangulated hernia	2	Nephrectomy	2
Hydrocele operation	3	Suprapubic cystotomy	9
Haemorrhoidectomy	10	Nephro-lithotomy	1
Thyroidectomy	3	Cystoscopies	50
Minor procedures	123		80
Mastectomy	4	*Orthopaedics*	
	353	Smith-Petersen pinning	9
Paediatric surgery		Open reduction of fractures	9
Rammstedt's operation	1	Meniscectomy	7
Laparotomy	1	Tendon repairs	18
Appendicectomy	16	Minor procedures, including fractures	101
Hernia repair	4		144
Operation for undescended testes	4	*E.N.T.*	
Circumcision	22	Tonsillectomy	82
Fractures, etc.	19	S.M.R.	14
	67	Intranasal antrostomy	5
Dentals		Others	11
In hospital	7		112
In dental surgery	300	*Ophthalmic*	
	307	Squint correction operation	5
		Iridectomy	1
		Excision of eyeball	1
		Needlings	3
			10

sufficient except for cases involving thoracic surgery and neurosurgery which are referred to specialized units in Belfast. The work done, therefore, is a fair sample of general anaesthetic practice (see table I).

TECHNIQUES

Evolution of technique.

In our earliest cases we employed the original method described by Johnstone, 5 litres each of nitrous oxide and oxygen flowing over halothane in the trichloroethylene bottle of a Boyle's machine, via a Magill's rebreathing attachment, to the patient. This proved so wasteful of halothane that we soon changed to (2) a semi-closed circuit including a Waters canister. A 50/50 mixture of nitrous oxide and oxygen at a rate of 2–4 litres per minute was used to vaporize halothane in the trichloroethylene bottle. Satisfactory anaesthesia was produced with considerable economy. However, as the Waters canister proved cumbersome it was replaced by (3) the Coxeter-Mushin circle absorber into which was fed the same anaesthetic mixture as in method (2). Convenience led us to adopt this as our standard technique, and it was used in every case for some weeks. During this time we gained experience, some facility in the use of the new agent, and confidence in the accuracy of the claims made by those who had introduced it into clinical anaesthesia. The only difficulty we encountered was an economic one. Halothane is expensive, and we soon found that our consumption of it was greater than could be justified.

Following Marrett's paper, we decided to employ a closed circuit technique (4). Boyle Mark II and Coxeter-Mushin circle absorbers were available and both gave excellent results. Unfortunately halothane caused some of the washers, gaskets, and other components to deteriorate, and two of our machines were rendered unserviceable. Specially made spare parts of more resistant materials had to be fitted before we could continue with our closed circuit series. Full details of our technical problems and an account of their solutions appear in another paper (*Brit. J. Anaesth.*, this issue, p. 338).

Detailed techniques at present used (table II).

In all cases atropine sulphate only is used for premedication.

TABLE II

Showing number of cases anaesthetized by various techniques

Total number of cases 1361

Technique	No. of cases
Semi-open Boyle 8–10 litre flow	125
Semi-closed with absorption 4 litre flow	56
Closed circuit 500 ml flow	880
Walton machine (dental cases)	300

(1) For infants and young children:

About 1 inch of halothane is placed in the trichloroethylene bottle of the Boyle's machine and a gas flow of 6–8 litres per minute of nitrous oxide-oxygen 50/50 delivered via a Magill's rebreathing attachment to the patient with or without an Ayres T-piece. With the plunger fully withdrawn the bottle control is gradually over 2–3 minutes advanced to "full on". When anaesthesia has been established the control lever can be returned to the half-way mark for maintenance.

(2) For older children:

The Coxeter-Mushin circle absorber is used, the halothane level in the vaporizer being kept below the bottom of the copper vanes. The soda lime must be renewed every 2½ hours to ensure efficient absorption. With the halothane control at zero a flow of 10 litres per minute of nitrous oxide is delivered to the facepiece which is held close to, but not against, the child's face. When amnesia has been produced, the nitrous oxide is turned off, the rebreathing bag emptied and filled with oxygen, and the mask firmly applied. With the soda lime control turned "full on" and 500 ml of oxygen per minute flowing, the vaporizer control is turned "¼" on. After a few breaths this is gradually advanced to "½" on and kept there until the jaw relaxes, when an airway or endotracheal tube can be inserted and the control returned to half way between the "¼" and "½" marks. This setting can usually be left untouched throughout the operation.

(3) Adults:

For out-patients and for elderly, debilitated, shocked, or very ill patients a pure halothane induction is used, employing the circle absorber.

With the rebreathing bag filled with oxygen, the soda lime in circuit, and 500 ml of oxygen per minute flowing, the mask is applied to the face and the vaporizer control turned to "¼" on. After 8–10 breaths the control is gradually advanced to "½" on. Automatic respiration and relaxation of the jaw usually occur in 2–3 minutes, but in more robust patients a mild stage of excitement may require the vaporizer control to be advanced to the "¾" mark. When anaesthesia supervenes the control is returned to the "½" position, and finally to half way between this and the "¼" mark.

Patients of average fitness are normally given a sleep dose of thialbarbitone sodium (3–7 ml of 10 per cent solution) followed by 50 mg of suxamethonium, if immediate intubation is intended. We then proceed as in method (3), assisting respiration until spontaneous breathing returns. If intubation can be deferred until the jaw relaxes under halothane, suxamethonium is completely unnecessary.

SIGNS OF ANAESTHESIA

In surgical anaesthesia with halothane the skin is pink and dry. The superficial veins of the extremities are dilated. The pupils are fixed, contracted and central, and the skeletal muscles extremely relaxed, the jaw muscles being among the first to become flaccid. Respiration is automatic, rather shallow, and faster than normal (30–50 per minute). Bradycardia (p.r. 40–60 per minute) and hypotension (systolic pressure 70–90 mm Hg) are a constant finding but appear to have no alarming significance.

If anaesthesia lightens, respirations become deep and more purposeful, eye movements appear, and reflexes quickly return causing flinching and coughing.

In deepening anaesthesia, however, the respirations become progressively more shallow, the pupils dilate, and the blood pressure tends to fall as respiratory arrest is approached.

CONDUCT OF ANAESTHESIA

Owing to variations of individual susceptibility to halothane and to differences in the efficiency of apparently identical vaporizers, rule of thumb instructions can only provide a rough guide to procedure. The exact depth of narcosis can be deduced at any moment from the physical signs exhibited by the patient, and can be lessened or increased in the course of a few breaths by altering the vapour concentration of halothane in the mixture being inhaled. This extreme flexibility is one of the most valuable attributes of halothane anaesthesia.

Muscular relaxation is so complete that most abdominal operations can be completed with spontaneous respiration. If very deep relaxation or a completely quiet abdomen is demanded it can be produced either (*a*) by injection of 50 mg of suxamethonium intravenously followed by fractional doses as required, or (*b*) by increasing halothane concentration with the circle vaporizer set at "¾" on.

In either case, as soon as breathing has almost ceased the rebreathing bag should be emptied and filled with oxygen and the vaporizer control turned to zero before inflating the patient's lungs. If this precaution is not taken too high a vapour concentration will be built up, anaesthesia will deepen still further, and spontaneous respiration will not return until the excess halothane has been washed out of the blood by artificial respiration with oxygen at a flow rate of 5 litres per minute. Fears expressed that a lethal concentration of halothane vapour would build up during closed circuit anaesthesia have proved groundless in the case of the Coxeter-Mushin absorber. In no case where the vaporizer control has been kept at the "½" mark or less has any progressive deepening of anaesthesia taken place even in cases where the control has been left untouched for nearly two hours.

Towards the end of long closed circuit anaesthetics nitrogen replacement should be effected by admitting air to the circuit to avoid post-anaesthetic pulmonary collapse.

As halothane consumption continues at a rate of 6–10 ml per hour during maintenance, we believe that halothane vapour must percolate quickly through the thin rubber of the hoses and rebreathing bag.

To study this problem we selected a number of cases in which cuffed endotracheal tubes had been passed, and all obvious mechanical leaks eliminated from the closed circuit. In each case, when the operation was nearly over, we turned off the vaporizer and cut the oxygen supply from 500 ml per minute to the estimated basal re-

quirement of the patient. The rebreathing bag was then partly emptied and the exhaust valve shut, thus completely separating the circulating gases from the outer air.

In every case progressive lightening of the anaesthesia became obvious after a few minutes.

As a result of these observations we decided to accept the fact that the rubber components of the circle absorbers in use are extremely permeable to halothane vapour. This property affords valuable protection against the unintentional and insidious deepening of anaesthesia which might otherwise occur.

POSTOPERATIVE OBSERVATION

Recovery from halothane is rapid. The reflexes normally return within 5 minutes and consciousness within 20 minutes after stopping the anaesthetic even following operations lasting up to 3 hours.

Nausea and vomiting sometimes occur but are of much shorter duration than after other agents. Patients frequently feel hungry and enquire anxiously about their next meal shortly after returning from theatre.

We agree with Johnstone that postoperative shock is much less severe in patients given halothane than in similar cases anaesthetized by the balanced technique.

SPECIAL INDICATIONS FOR USING HALOTHANE

Though halothane has been adopted as a routine general purpose anaesthetic in our practice, certain types of cases seem particularly to benefit from its use.

(1) Poor risk patients—elderly, ill, toxic, or shocked. These are the kind of patients who figure all too frequently in case reports of persistent curarization when techniques requiring relaxants have been used. They do amazingly well with a pure inhalation technique, especially as adequate relaxation can be obtained without giving relaxants. It is of great advantage to such patients as presumably no breakdown products of the anaesthetic are left to embarrass further their excretory organs.

(2) Obstetric cases. Our small series of Caesarean sections has led us to believe that halothane may become a very useful agent for obstetric anaesthesia, both in hospital and domestic practice. It produces quick pleasant induction without vomiting, early muscular relaxation and quick recovery. Uterine contraction and retraction are not affected. The infants are not born with respiratory depression due to the anaesthetic, and usually cry readily.

(3) Outpatients. While it is potent enough to subdue even robust individuals safely, the quick recovery and freedom from unpleasant after-effects make it invaluable in the casualty room.

(4) Otolaryngological cases. Minor procedures in children, such as tonsillectomy, adenoidectomy and antrum puncture are greatly facilitated by the easy induction, quick jaw relaxation and the speedy recovery. In adults the relatively bloodless field afforded is audibly appreciated by the surgeon.

(5) Ophthalmology. A feature of halothane anaesthesia is the progressive decrease in intra-ocular tension as narcosis deepens. Our ophthalmologist has found this fact and the recovery without coughing or retching to be especially valuable in certain cases. She comments upon the marked reduction in bleeding, especially notable in extra-ocular operations.

(6) Dentistry. In more than 300 cases we have used halothane (vaporized in a Rowbotham's bottle) to supplement nitrous oxide-oxygen anaesthesia in the dental chair, using a Walton intermittent flow machine. A smoother anaesthetic, with better jaw relaxation and quicker recovery, can be obtained than when trichloroethylene is used in the same way. An added advantage is the higher percentage of oxygen permitted by the greater potency of halothane. The absence of any increase in secretion of saliva and mucus due to the anaesthetic makes conditions more pleasant for both dentist and anaesthetist.

Though our series of cases has included some difficult clearances demanding extended operating time we have never felt in the least apprehensive about the patients. The temporal pulse remains steady and full, the colour good, and the respirations automatic and deep.

CLINICAL ASSESSMENT

Halothane has been used in nearly every case anaesthetized by the writers for more than seven months. About 1361 operations have been done,

the ages of the patients varying from a few days to more than 90 years and their conditions from the robustly healthy to the almost moribund. Considering this experience, we know of no other anaesthetic or combination of anaesthetics which can give results so acceptable to the three individuals principally concerned in a surgical operation.

The patient has a quick easy induction, a safe anaesthesia, and a quick recovery with few unpleasant after-effects.

The surgeon has a pink spontaneously breathing patient who is well relaxed, shock resistant, and less haemorrhagic than usual.

The anaesthetist is possibly the most satisfied of the three. He has the pharmacological effects of only one drug to consider and can control the depth of anaesthesia almost from breath to breath to meet the needs either of the surgeon or the patient. Above all he is absolved from the necessity of watching the condition of his patient slowly deteriorate under the combined attack of surgical shock and long acting narcotics in spite of every available supportive measure.

Economically, when closed circuit technique is employed, the saving affected in nitrous oxide, oxygen, narcotics and relaxants is almost enough to neutralize the comparatively high cost of halothane, but this argument is only useful for soothing agitated hospital pharmacists.

We believe that any anaesthetist who gives halothane a fair trial will become enthusiastic.

SUMMARY

The administration of halothane ("Fluothane") in a series of 1361 cases including most general surgical procedures is described. Special reference is made to the use of halothane in the ether vaporizer of closed circuit apparatus. The clinical findings and the special advantages of halothane in particular operations are discussed.

ACKNOWLEDGMENTS

We are deeply indebted to Mr. John Beale, of Imperial Chemical Industries Ltd., for his help in making the technical resources of his organization available to us and for the personal interest he has taken in our work. Mr. G. Donnelly, B.Pharm., Imperial Chemical Industries Ltd., medical representative in Northern Ireland, has been tireless in effecting liaison with the various departments of his firm on our behalf. Mr. J. Cockton, Ph.C., Department of Pharmacy, Imperial Chemical Industries Ltd., carried out many investigations at our request, and arranged for the fabrication and fitting of the various special components required for our closed circuit units. We are also indebted to Dr. K. G. Green, I.C.I., for helpful advice and supplies of halothane.

Finally we would like to thank our surgical colleagues for the patience they showed during our early cases. We are pleased to accord that the good-humoured scepticism they then displayed has now given way to solid approval.

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MODIFICATION OF THE COXETER-MUSHIN CIRCLE ABSORBER UNIT FOR USE WITH HALOTHANE IN THE CLOSED CIRCUIT

BY

T. A. BROWN AND M. A. WOODS

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IN a previous article (Brown and Woods, *Brit. J. Anaesth.*, this issue, p. 333) we have referred to technical difficulties experienced with the machines we used in our closed circuit cases.

As it seems possible that others working with similar apparatus may wish to employ halothane in this way, we thought that some account of the troubles encountered and the modifications required might be of interest.

The Boyle II and Coxeter-Mushin units at our disposal were designed for use with di-ethyl ether or cyclopropane, both of which are relatively inert chemically when mixed with the oxygen, nitrogen, carbon dioxide, and water vapour flowing through the circle absorber with each respiration of the patient.

Moist halothane vapour under the same conditions is chemically active and tends to destroy many of the rubber and synthetic materials used for gaskets and washers in anaesthetic apparatus. Certain metals are also attacked and corroded—notably brass, solder, and certain alloys of aluminium. It was corrosion of the brass control drum of the vaporizer on the Boyle II unit which caused it to become immovable and forced us to abandon this machine for closed circuit work early in the series.

Fortunately the moving metal parts of the Coxeter-Mushin unit proved sufficiently resistant for our purpose, though there was evidence of corrosion in the ether container. The first failure with this machine was the rubber washer forming the joint between the ether vaporizer and the body of the unit, which softened, expanded and soon became useless. Frequent replacements were required. Next in succession was the washer sealing the lower end of the sight gauge glass, which failed and allowed liquid halothane to run out. Next came the gasket between the two halves of the carcase of the unit which softened and became extruded inside the machine. Detached portions of this caused anxiety by threatening to block the ports of the vaporizer. As may be imagined, at this stage in our work we felt a little discouraged. Two of our machines were out of action, and the others had to be carefully watched when in use in case of sudden failure.

We were fortunate enough to seek the advice of Mr. J. Cockton of the Department of Pharmacy, Imperial Chemical Industries Ltd. He provided a toughened glass replacement for the metal ether container of the unit, and took the unserviceable machines for examination by technical experts of Imperial Chemical Industries Ltd. and the British Oxygen Company. As a result of the information obtained further consultations took place and the following modifications were decided upon:

(1) The metal ether container was replaced by one of similar size and shape made of toughened laboratory glass. A filler with a ground glass stopper was provided. We do not empty this container between operating sessions—firstly because of the risk of breakage, and secondly because there is a noticeable loss of halothane by evaporation on decanting (fig. 1).

(2) The bakelite or metal retaining ring holding the washer which seals the gap between the ether container and the unit has been removed. The rubber washer is retained but is protected from contact with halothane vapour by a thin channel shaped moulding of Fluon (a halothane resistant plastic). Fluon by itself is too hard to provide a gastight joint (fig. 2).

(3) The gasket between the two halves of the carcase of the unit has been replaced by a sandwich of Fluon and Gatan leather—the latter,

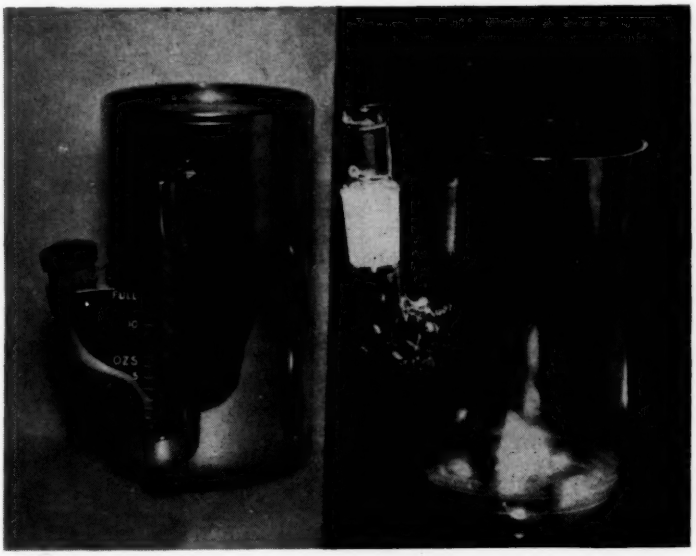

FIG. 1
Showing toughened glass container (see text) and standard metal ether vaporizer.

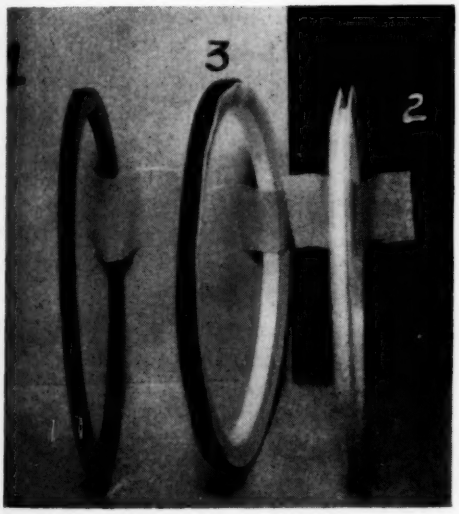

FIG. 2
Showing (1) standard rubber washer, (2) "Fluon" plastic cover, (3) rubber washer inserted into "Fluon" cover.

which is halothane resistant, and softer than Fluon, to allow bedding together to take place.

These modifications appear to have eliminated the faults which our misuse of the machines had produced. No further faults have developed, and we are satisfied that the Coxeter-Mushin absorber unit properly modified is perfectly suitable for the closed circuit administration of halothane.

The British Oxygen Company informs us that they are willing to undertake the above modifications for those wishing to use the Coxeter-Mushin unit for halothane anaesthesia.

Any anaesthetist wishing to experiment with closed circuit halothane without radically altering his machine may care to adopt the following procedure:

(1) After screwing off the copper vane assembly remove the rubber washer and its retaining ring (secured by three grubscrews) between the ether vaporizer and the carcase of the unit. Cut a similar washer from polythene sheet of suitable thickness ($\frac{1}{16}$ to $\frac{1}{8}$ inch) but make it wide enough to cover the three grubscrew holes. The grub-

screws are then used to retain it in position. The washer must fit exactly into the recess in the unit to avoid leakage.

(2) Carefully remove the gauge glass from the ether container. Take out the synthetic rubber washers below and above it and replace them with polythene—the old washers can be used as patterns for cutting the new.

(3) Replace the ether container, put in a few ounces of halothane, and test for leaks by opening the vaporizer control to full on, filling the rebreathing bag with air or oxygen, and squeezing the bag firmly with the opening at the mask connection occluded by the other hand, the hose connections having previously been forced tight. Any leak detected must be eliminated before using the machine.

The gasket between the two halves of the carcase of the unit may be left in situ. If it causes trouble it is easily replaced with a sheet of polythene or polyvinyl chloride. This sheet should be placed in position and the unit assembled, the various openings being cut out afterwards with a fine sharp scalpel. No adhesive or jointing compound is required. Halothane left in the metal ether container soon becomes brown and muddy-looking. This is due to dissolved metallic salts and oxydized thymol, and is of no clinical significance. We have been assured that no volatile impurities occur.

ACKNOWLEDGMENT

We are indebted to Mr. J. MacGowran, M.S.R., for the photographs of the apparatus.

ON CHLOROFORM AND OTHER ANÆSTHETICS

THEIR ACTION AND ADMINISTRATION

BY

JOHN SNOW, M.D.

Licentiate of the Royal College of Physicians

(*Continued from page 297*)

The chloroform has occasionally to be repeated in tooth-drawing before the operation is completed, especially in cases where several teeth require to be extracted. When this is the case, I always reapply it as soon as the patient begins to show signs of feeling the operation, without waiting till he recovers his consciousness. In many cases, however, a number of teeth are extracted without any repetition of the chloroform; and in the instances in which as many as fifteen, seventeen, or nineteen teeth were extracted at one operation, it was chiefly because the first application of the vapour enabled the dentist to take out such a number, otherwise, in most of these cases, a number of the teeth would have been left for a succeeding operation. It has occasionally happened, however, that the chloroform has required to be repeated, once or twice even, for the extraction of a single stump. When the chloroform is repeated once or twice, it is generally a longer time before the patient is able to leave the dentist's house. I always request the patients who are operated on at the dentist's, to drive home, as it is not advisable to walk, or use any exertion for an hour or two after the action of chloroform. Indeed, the patient is usually disinclined for any exertion for twenty minutes or half an hour after the influence of this agent, and sometimes for much longer; although I have seen a patient mount the box of a sort of dog-cart, and drive himself away, within five minutes after having several teeth extracted whilst he was in a state of complete insensibility from chloroform.

I have administered chloroform in a great number of cases for the destruction of the nerves of the teeth. The patient requires to be made as insensible in this operation as in tooth-drawing.

Secondary Hæmorrhage after Operations. The hæmorrhage which occasionally comes on several days after an operation, from sloughing, ulceration, or the non-formation of a coagulum in an artery, is probably as liable to occur now as formerly; but I believe that hæmorrhage, a few hours after an operation, is much less frequent since the practice of narcotism by inhalation. Before this practice, it was extremely common for the patient to faint during an operation, when the bleeding of the smaller arteries stopped, and they escaped the ligature, to break out in hæmorrhage occasionally afterwards; but under the influence of narcotic vapours it is unusual for the patient to faint, and consequently every vessel which is capable of bleeding is tied during the operation.

CHLOROFORM IN PARTURITION

When the practice of inhalation in midwifery was first introduced by Dr. Simp-

son, he very naturally adopted the plan which is usually followed in surgical operations, making the patient unconscious at once, and keeping her so to the end of the labour. It was soon found, however, by other practitioners, that this is not necessary; and, indeed, it would not be safe in protracted cases. Drs. Murphy and Rigby were, I believe, amongst the first to state, that relief from pain may often be afforded in obstetric cases, without removing the consciousness of the patient; and I soon observed the same circumstance.* Some persons, indeed, have alleged that the pain of labour can always be prevented, without making the patient unconscious of surrounding objects; whilst others have asserted that no relief can be afforded unless unconsciousness be induced. But both these opinions are directly opposed to experience. There are comparatively few cases in which the suffering can be prevented throughout the labour without interfering with consciousness, although there are very many cases in which it can be in this way prevented in the early part of the labour. This difference depends, in some measure, on the constitution of the patient, but chiefly on the severity of the pain to be prevented. It is in accordance with what is observed in medical and surgical cases, that the pain should be removed, in some instances, without abolishing consciousness, and that in other instances it should not; for, in certain cases of neuralgia, the pain is so severe, that no material relief can be obtained by chloroform as long as consciousness is retained; and in surgical operations, although it now and then happens that the minor and concluding parts of an operation, such tying vessels and introducing sutures, can be performed without pain, whilst the patient is consciously looking on, a free incision in the skin can hardly ever be made, under similar circumstances, without pain.

With regard to the cases of labour in which chloroform may be employed, it will be readily conceded that, in cases where the pain is not greater than the patient is willing to bear cheerfully, there is no occasion to use chloroform; but when the patient is anxious to be spared the pain, I can see no valid objection to the use of this agent, even in the most favourable cases. The benefits arising from chloroform in severe cases of labour are experienced in a lesser degree in favourable cases; and the patient may be fairly allowed to have a voice in this, as in other matters of detail which do not involve the chief results of the case. The determination of the kind of labours in which chloroform should be used, or withheld, is really a matter of not much importance, because, as we pass from cases that are severe and protracted to those which are short and easy, the quantity of chloroform that is used, and the amount of diminution of the common sensibility, and of interference with the mental functions, become so trifling, that very little remains about which to hold a discussion. Indeed, from what I have observed of the continued use of this agent in medical cases, and its use by healthy persons for experiment, I believe that the quantity which is inhaled in a short and easy labour might be continued daily for an indefinite period, without appreciable effect on the health.

The above remarks apply also, in some

* London Journal of Medicine, vol. i, pp. 54, 976.

measure, to the question as to the period of the labour when the exhibition of chloroform should commence; for, in proportion as the pains are feeble, it must be more sparingly administered. The most usual time when the accoucheur and I have determined that the inhalation should be commenced, has been when the os uteri was nearly dilated to its full extent, and the pains were taking on an expulsive character. In many of the cases which I have attended, it has, however, been commenced much earlier; for the suffering caused by the dilating pains in the first stage of labour is often very great, and the chloroform is consequently of the utmost service when employed at this time.

As regards the manner of giving chloroform, I shall first allude to cases not requiring manual or instrumental assistance. In such cases, when it has been determined to resort to inhalation, the moment to begin is at the commencement of a pain; and the chloroform should be intermitted when the uterine contraction subsides, or sooner, if the patient is relieved of her suffering. It is desirable to give the chloroform very gently at first, increasing the quantity a little with each pain, if the patient is not relieved. The practitioner easily finds, with a little attention, the quantity of vapour which it is desirable to give at any stage of the labour, and in each particular case; his object being to relieve the patient without diminishing the strength of the uterine contractions and the auxiliary action of the respiratory muscles, or with diminishing it as little as possible. At first, it is generally necessary to repeat the chloroform at the beginning of each "pain"; but, after a little time, it commonly happens that sufficient effect has been produced to get the patient over one or two uterine contractions without suffering, before it is resumed.

The external evidences of the uterine contractions continue as before, when the patient is rendered unconscious by chloroform; and the muscles of respiration are called freely into play, to assist the action of the uterus in the second stage of labour. The aspect of the patient under these circumstances, is generally that of one who is suppressing the expression of her sufferings; and any relative or friend who comes in, without knowing that chloroform has been given, begins to praise the unconscious patient for her fortitude. On some occasions, indeed, there are groans and cries, as of suffering; but the mind being unconscious of pain, it can hardly be said to exist.

It may be remarked, that complete anæsthesia is never induced in midwifery, unless in some cases of operative delivery. The diminution of common sensibility to a certain extent, together with the diminution or removal of consciousness, suffice to prevent the suffering of the patient during labour; and she never requires to be rendered so insensible as in a surgical operation, when the knife may be used without causing a flinch or a cry. The nerves of common sensation must be allowed to retain their functions to a certain extent during labour; otherwise the assistance of the respiratory muscles, which consists of reflex action, or "motion arising from sensation, without the aid of volition" would not take place, even if the contractions of the uterus should still continue.

The effects of chloroform on the brain should not be carried during labour beyond what I denominate the second degree of narcotism, or that condition in which the mental functions are diminished, but not altogether suspended, except when the effect of the vapour is associated with natural sleep. The patient under the influence of chloroform to this extent, has no longer a correct consciousness of where she is, and what is occurring around her, but is capable of being aroused to give incoherent answers, if injudiciously questioned. In this state, the patient will sometimes assist the labour by bearing down voluntarily, if requested to do so, and be otherwise obedient to what is said; and by withholding the chloroform for a few minutes, she at any time becomes quite conscious. As a general rule, it is desirable not to hold any conversation whilst the patient is taking chloroform, in order that her mind may not be excited. The plan mentioned above, of giving the chloroform very gently at first, also has a tendency to prevent its causing mental excitement, the patient coming gradually under its effects. In surgical operations, excitement of the mind can nearly always be avoided by carrying the patient pretty rapidly into a state of insensibility, in which the mental functions are necessarily suspended. But in the practice of midwifery, it is not allowable to cause a state of coma or insensibility, except in certain cases of operative delivery, hereafter to be mentioned.

I nearly always employ, in obstetric cases, the inhaler that I use in surgical operations. There is not the same necessity for an accurate means of regulating the proportion of vapour in the air which the patient is breathing during labour, where but a trifling amount of narcotism requires to be induced, as in surgical operations, where a deeper effect is necessary; still I find the inhaler much more convenient of application than a handkerchief, and it contains a supply of chloroform which lasts for some time, thereby saving the trouble of constantly pouring out more. When I do administer chloroform on a handkerchief during parturition, I follow the plan of putting only ten or fifteen minims of chloroform on the handkerchief at one time.

The quantity of chloroform administered during any one pain, never exceeds a very few minims; but the quantity used in the course of a protracted labour is often considerable. I have several times used from four to six ounces; and in one case, at which I was present the greater part of the time, seventeen fluid ounces of chloroform were used with the inhaler, which would produce as much effect as three or four pounds used on a handkerchief. The inhalation was continued with intermissions over a period of thirty-one hours. The patient was unconscious during the greater part of the last five or six hours, but previously to this, her constant complaint was that she had not enough chloroform. She was the wife of a physician, was thirty-seven years of age, and in her first confinement. The membranes ruptured early. The labour was natural, but there was excessive sensibility. The first twenty-six hours of intermitted inhalation were during the first stage of labour.

Chloroform can be best applied when there is an additional medical man, who has not to attend to the ordinary duties of

the accoucheur; but it can be given very well by the accoucheur himself, so as to save the greater part of the suffering of labour; although he perhaps cannot always administer it in the perfect way in which he could, if he had no other duties to divide his attention.

It is probable that the use of chloroform has no particular influence over the duration of labour, in the whole number of cases in which it is employed; but individual labours are occasionally either retarded or quickened by it, according to circumstances. In some cases, the chloroform, even when very moderately employed diminishes both the strength and the duration of the uterine contractions, and prolongs the interval between them, thereby making the labour somewhat longer — a matter of no consequence, however, as the patient is not suffering in any way. In other cases, the inhalation causes the uterine action to become stronger and more regular, by removing the excess of sensibility by which it has been interfered with. This occurs more particularly in the first stage of labour. In some cases, also, the chloroform seems to act as a direct stimulant to the uterine contractions, increasing their force and frequency—a circumstance at which we need not be surprised, when we remember that both opium and brandy, in moderate quantity, often act in the same manner. Chloroform has also the effect of promoting the dilatation of the os uteri in many cases even when no rigidity exists; and when there is rigidity of the os uteri, the inhalation is of the utmost service, and shortens labour very much. This is the case, also when there is rigidity of the perineum.

When the forceps have to be applied, it is desirable to make the patient insensible, as if for a surgical operation just before they are applied; and to leave off the chloroform as soon as they are introduced, in order to allow of the uterine action to return, and assist in the delivery. I have always found the action of the uterus return immediately after the forceps were introduced; and where the child was not delivered at once, I have continued the chloroform in sufficient quantity to keep the patient unconscious, whilst allowing the uterine contractions to continue.

I have administered chloroform on nine occasions in which the forceps were applied; in four of the cases, I was sent for in consequence of the operation being required; and in the other five cases, I was in attendance from an early part of the labour, and had administered chloroform more or less for some hours before the forceps were applied. They were applied in three instances by Dr. Murphy, twice by Dr. Ramsbotham, and in the other cases by Drs. Farre, Frere, and Thudichum, and Mr. Peter Marshall.

I have administered chloroform in two cases of craniotomy, both of which were performed by Dr. Murphy, on account of deformity of the pelvis. The amount of chloroform scarcely requires to be increased during this operation beyond what would be given according to the strength of the pains which may be present at the time.

In the operation of turning the child, the mother requires to be made quite insensible, in order that the uterine contraction may be made entirely suspended till the legs of the child are brought down,

when the inhalation should be discontinued to allow the contraction of the uterus to return. I have notes of six cases of turning the child, in which I have administered chloroform. The first case, which occurred in 1848, was one of natural presentation, in which turning was performed by Dr. Murphy, on account of narrowness of the pelvis, and the impossibility of applying the forceps; the introduction of the hand was difficult on account of want of space, but the uterus offered no resistance. Dr. Murphy has related the case. Three of the other instances of turning were performed by Mr. French, in cases which had been attended by midwives, and the membranes had been ruptured for several hours. The shoulder and part of the chest were in each case pressed down into the pelvis, and the pains were very strong; yet under a full chirurgical dose of chloroform, the child was turned as easily as if the membranes had not been ruptured. In the first of these three cases, the child was dead before the operation commenced. In the other two, it was born alive. In the last case, the membranes had been ruptured for ten hours before the operation was performed. After the child was delivered, there was found to be a second child presenting naturally, but I did not stay to give any more chloroform. The fifth case of turning was performed in a case of elbow presentation by Mr. Peter Marshall. The membranes had been previously ruptured. I administered chloroform, also for Mr. Marshall, in a case where the hand was presenting below the head; he raised it above the head, and as it did not come down again when the pains returned, the labour was allowed to pursue its natural course, and terminated favourably in two or three hours, the child being alive. The chloroform was not continued after the operation was performed. The remaining case of turning was performed by Mr. Tegart, of Jermyn Street. I was in attendance with him from an early stage in the labour, and the operation was performed before the membranes were ruptured.

I administered chloroform, in 1849, in a case in which Dr. Murphy had to make an artificial os uteri. The patient was, of course, made quite insensible as for any other surgical operation; and the vapour was continued afterwards in a modified degree till the labour was completed.

On December 26th, 1850, I was requested by Mr. Cooper, of Moor Street, Soho, to assist him in a case of retention of the placenta. The patient had given birth to a child two hours before, and Mr. Cooper had introduced his hand, but had been unable to bring away the placenta, on account of firm contraction of the uterus in a sort of hour-glass form. On the chloroform being administered, the hand was easily introduced, and the placenta detached, and extracted. There was very little hæmorrhage.

In some of the many cases at which I have met Dr. Cape, premature labour was induced about the eighth month of utero-gestation, by rupturing the membranes, on account of deformity of the pelvis.

In a case attended by Mr. Cantis, the patient was suffering from osteo-sarcoma of the bones about the shoulder. Dr. Fergusson was present during the latter part of the labour. The lady lived a few weeks after her confinement.

(To be continued)

CORRESPONDENCE

DECAMETHONIUM IODIDE: A REAPPRAISAL

Sir,—I have read with great interest Dr. Murray Lawson's reappraisal of decamethonium iodide, particularly as my colleagues and I have recently had striking proof of the usefulness of this drug in the treatment of a case of tetanus, a full report of which we hope to publish shortly.

We started to treat the child with chlorpromazine, but although major spasms were prevented, the patient's muscles were still tonically contracted. He lay in obvious discomfort, with back arched and head retracted. With the administration of decamethonium iodide, the hypertonus was completely abolished and the patient, a boy of four, lay comfortably in a prone position.

One of the most satisfactory features of decamethonium iodide is that it is possible, with this drug, to achieve relaxation of the patient's muscles without significantly depressing respiration. The patient in this case was treated with decamethonium iodide for fourteen days. Spontaneous respiration was maintained throughout and there were no chest complications. I know of no other drug with which this could have been achieved with such ease and freedom from untoward effects.

I join with Dr. Murray Lawson in hoping that the manufacturers will continue to market this most useful drug, and that it will find its true place in anaesthesia.

R. McD. S. Keir
Royal Infirmary, Dumfries

PATIENT CYCLED RESPIRATOR

Sir,—After we submitted our paper on a "Patient-Cycled Respirator" (*Brit. J. Anaesth.* (1958), **30**, 32) we started investigating the possibility of designing a transistor timing circuit in place of the commercial timer referred to, and work upon this and on various projects arising out of it have been so promising that although it is hoped to publish full details in due course we felt that some comments on our more recent work might be of interest.

First, some modifications were made to the respirator described in the paper. It had rarely been found necessary to use a stroke volume in excess of 500 ml, so the $1\frac{1}{2}$ gallon bag was replaced by one of 750 ml capacity—this being two air-bed inflators overlaid by one corrugation and cemented. The latching relay was replaced by a bi-stable relay operated directly from the trigger and a transistor timer used.

These modifications allowed the whole assembly to be mounted in a single case and it was therefore a second, and much more compact, model of the respirator that was demonstrated to the Symposium at Leeds in February.

At the same time the possibility was investigated of designing an infant respirator of variable time and pressure using transistors, and an experimental model incorporating two midget transistor timing units which operated alternately and governed the inspiratory and expiratory periods respectively was also shown at Leeds. This again used a trigger in exactly the same manner as that described in the paper.

From these preliminary experiments it seems clear that transistors of the types now coming on the market will prove extremely valuable in the design of timing units for such purposes as respirators and two types of circuit in particular are being studied at the moment.

The first type of circuit uses two power transistors in what is, in effect, a very low frequency multivibrator, provision being made for a photoelectric trigger to cause one of the transistors to conduct immediately on inspiration irrespective of the state of charge of the condensers in the circuit. The second type of circuit uses two flip-flops in a ring of two circuit, with a third operated by the trigger. The two timing flip-flops are so arranged that they operate alternately, the one controlling the inspiration time, during which the solenoid valve is open, and the other governing the interval time, i.e. the period during which the solenoid normally remains closed. If, however, the trigger operates during this period it overrides the delay timer, and immediately initiates the inspiratory phase. The period of operations of

the two flip-flops is determined by the time taken by a condenser across the input to discharge through a variable resistor.

The respective advantages of these two circuits are in general that, in the first, the number of components is minimal and more particularly no relays are required (the solenoid valve being operated directly by a power transistor), thus the device is free from any possibility of sparking at contacts. The range of variation of periods is, however, rather limited. In the second circuit in which separate timing units are used, a very wide range of inspiratory and interval periods may easily be obtained and there is, of course, no interaction between them. At the moment relays are used as a matter of convenience but this is obviously not fundamental.

In a typical respirator of either type the power consumption may be about 25 mA, plus perhaps 500 mA while the solenoid valve is open. For a normal inspiratory ratio this implies a mean current of 200 mA, at 18V which for emergency use can easily be obtained from dry batteries, as can the supply for the bulb in the trigger (200 mA at 3V). A self-powered attaché case respirator has therefore been built, with an improved form of trigger, and incorporating a small cylinder, with provision for using external gas and mains supplies as available. This trigger operates on an instantaneous flow rate of less than 1 litre per minute and does not present any obstruction to breathing so, as the expiratory valve "fails safe", even if both normal and emergency supplies of either gas or electricity fail, voluntary breathing is in no way impeded. Preliminary clinical trials suggest that this instrument will be very useful.

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